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Effectiveness and Safety of Orodispersible Budesonide for Eosinophilic Esophagitis: A Multicenter Real-World Study

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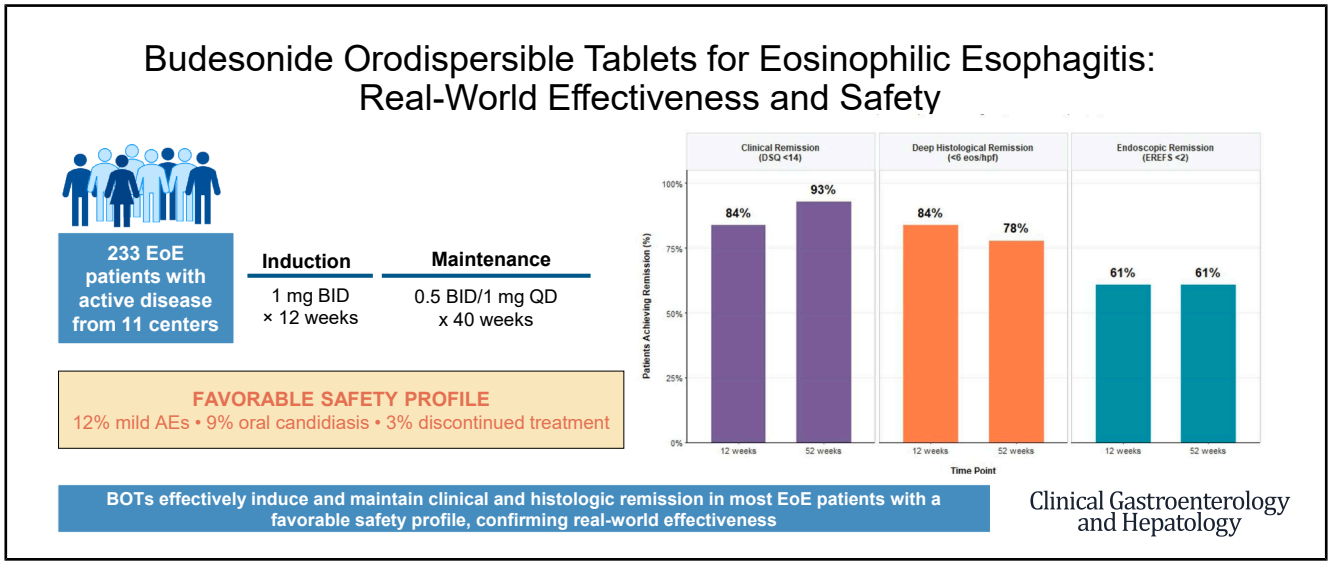

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Abbreviations used in this paper: **AE, adverse event; BOT, budesonide orodispersible tablet; DSQ, Dysphagia Symptom Questionnaire; EoE, eosinophilic esophagitis; EoE-QoL-A, Adult Eosinophilic Esophagitis Quality of Life questionnaire; eos/hpf, eosinophils per high-power field; EREF, Endoscopic Reference Score; HRQoL, health-related quality of life; MCID, minimum clinically important difference; PPI, proton pump inhibitor; RCT, randomized controlled trial; TC, topical corticosteroid.**

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BACKGROUND & AIMS: **Topical corticosteroids represent one of the effective first-line treatment options for eosinophilic esophagitis (EoE), and therapy with budesonide orodispersible tablets (BOTs) has been recently approved for the treatment of EoE and showed great efficacy in randomized-controlled clinical trials, however real-life data are lacking. Thus, we aimed to evaluate the effectiveness of treatment with BOTs in adult EoE patients in a real-life setting.**

METHODS: **In this prospective study, clinical, histologic, endoscopic, and safety measures were assessed. Patients underwent evaluation after the induction period (12 weeks) and up 1 year of treatment with BOTs. Dysphagia Symptom Questionnaires were used for symptoms; the Adult Eosinophilic Esophagitis Quality of Life questionnaire for quality of life; the Endoscopic Reference Score for endoscopic activity; eosinophilic peaks (eosinophils per high-power field) for histologic activity.**

RESULTS: **A total of 233 patients were enrolled and 203 completed the assessments after 12 weeks. Deep histological remission was achieved by 84% of patients, as well as clinical remission, associated with an improvement in quality of life. Eighty-six patients concluded 1 year of treatment, and 78% were still in deep remission, while 15% experienced a loss of histological response at treatment tapering. Primary nonresponders were 8%, and secondary nonresponders were 3%. No serious adverse effects were recorded. Only mild side effects related to drug assumption were reported by 28 (12%) of 233 patients, and the most common were oral symptoms.**

CONCLUSIONS: **Our real-world data confirm that BOTs are effective in inducing clinical and histologic remission in most EoE patients. The drug has a good safety profile, with side effects occurring only in a small number of patients.**

Keywords: Inflammation; Steroids; Therapy; Eosinophilic Esophagitis; Type 2 Inflammation.

Eosinophilic esophagitis (EoE) is a chronic, inflammatory, allergic antigen–mediated disease with a rising global prevalence over the past decade.[1] It is characterized by esophageal dysfunction symptoms, such as dysphagia and bolus impaction, along with esophageal eosinophilia (≥15 eosinophils per high-power field [eos/hpf]).[1] Other gastroesophageal symptoms, particularly in younger individuals, may contribute to misdiagnosis and diagnostic delay.[2–6] Diagnosis remains challenging due to the absence of noninvasive detection methods,[7] and requires the exclusion of other causes of esophageal eosinophilia.[8–11]

Dysphagia and food bolus impaction, often due to esophageal fibrosis, are the predominant symptoms significantly affecting patients' health-related quality of life (HRQoL).[12,13] The chronic inflammatory nature of EoE leads to esophageal dysfunction, remodeling, and dysmotility, necessitating targeted treatment.[14–18]

Pharmacological therapy targets disease pathogenesis based on clinical characteristics.[11,19,20] Anti-inflammatory treatments include proton pump inhibitors (PPIs), topical corticosteroids (TCs), and the recently approved monoclonal antibody dupilumab.[21–23] TCs are widely used in clinical practice due to their effectiveness in achieving and maintaining clinical, endoscopic, and histologic remission,[22,24–27] with a favorable safety profile.[20]

Until recently, TC treatment relied on off-label swallowed fluticasone propionate and oral viscous budesonide mixed with thickeners to form an aqueous gel.[1,26] However, their heterogeneous composition, variable dosing, and inconsistent administration have led to variable therapeutic outcomes.[23,28,29] A novel formulation of budesonide orodispersible tablets (BOTs) has been specifically developed for esophageal distribution, demonstrating efficacy in inducing and maintaining clinical and histologic remission.[30,31] Despite evidence from randomized controlled trials (RCTs) supporting BOT safety and efficacy, real-world studies remain limited to retrospective cohorts with small sample sizes.[32–34] This study aims to provide prospective real-world data on the effectiveness and safety of BOTs for both induction and maintenance therapy up to 1 year, as well as its impact on the quality of life of patients with EoE.

Materials and Methods

Study Design and Population

This prospective, multicenter, observational study was conducted across 11 medical centers from March 2023 to September 2024. Adults (18–80 years of age) diagnosed with EoE per international guidelines[1] were included if initiating BOT treatment for the first time, continuing for ≥12 weeks, and having active disease at index endoscopy (EREFS score ≥2 and ≥15 eos/HPF). The complete list of inclusion and exclusion criteria is included in the Supplementary Materials.

Procedures and Outcomes

At baseline, 12 weeks (T1), and 52 weeks (T2), assessments included: clinical symptoms using the Dysphagia Symptom Questionnaire (DSQ)[35]; endoscopic activity using the modified Endoscopic Reference Score (EREFS) with biopsies from 3 esophageal locations[11]; histological remission determined by eosinophil counts (eos/hpf); and HRQoL using the Adult Eosinophilic Esophagitis Quality of Life questionnaire (EoE-QoL-A). Safety was evaluated based on patient-reported adverse events (AEs).[36] A detailed description of assessment procedures and study outcomes is provided in the Supplementary Materials.

Statistical Analysis

Differences in proportions were compared using chi-square or Fisher's exact test. Unless otherwise specified, data are presented as mean ± SD. Non-normally distributed data were analyzed using Kruskal-Wallis and Mann-Whitney tests. Statistical significance was set at $P < .05$.

All statistical analyses were performed using STATA software, version number 18 (StataCorp). The sample size calculations are provided in Supplementary Materials.

Ethical Considerations

This study was approved by the Territorial Ethical Committee (5797/AO/23). All participants provided written informed consent before inclusion. The study was conducted in strict adherence to the approved protocol and in full compliance with the ethical principles outlined in the Declaration of Helsinki.

Results

Patient Enrollment

A total of 273 patients were recruited (81% males, 37 ± 13 years), but 15 were excluded due to disease remission at enrollment, and 24 were lost to follow-up. Thus, data were available for 203 patients at baseline and after 12 weeks. Subsequently, 1 patient was excluded for low compliance, 2 discontinued BOT due to AEs, and 27 did not undergo postinduction endoscopy. At 52 weeks, 86 patients completed all procedures; 110 missed the endoscopic evaluation, 5 stopped treatment due to AEs, and 2 were excluded for low compliance. The flow diagram of the study is presented in Supplementary Figure 1.

Baseline Characteristics

The demographic and medical history of the study cohort are summarized in Table 1. Most patients were male (n = 192 of 233 [82%]), with a mean age of 37 ± 14 years. The mean age at diagnosis was 32 ± 14 years, with dysphagia reported in 189 (81%) of 233 and food bolus impaction in 165 (71%) of 233. Most patients (n = 193 of 233 [83%]) had prior PPI treatment with 24% of them able to obtain clinical response, but endoscopic and histological remission were not achieved or maintained. None of the patients were previously treated with biologics, and only 30% were treated with off-label formulations of topical steroids. Sixty-nine (30%) of 233continued PPIs during induction and maintenance. At baseline, dysphagia and odynophagia severity were assessed using the DSQ score (28 ± 25), while the EoE-QoL-A score averaged 111 ± 36. All patients had active disease based on the EREFS score (3 ± 2). Histological assessment recorded eosinophilic peaks in the distal (31 ± 29), mid (28 ± 28), and proximal (37 ± 35) esophagus. Baseline demographic and clinical characteristics of the study population are summarized in Table 2.

What You Need to Know

Background

Eosinophilic esophagitis is a chronic type 2 inflammatory disease causing esophageal dysfunction. Budesonide orodispersible tablets are a targeted therapy, but real-world data on long-term efficacy and safety are limited.

Findings

After 12 weeks, 84% achieved deep histologic remission, with clinical improvement in 99% of symptomatic patients. At 1 year, 78% remained in remission, though 15% lost response after dose tapering.

Implications for patient care

Budesonide orodispersible tablets are highly effective for inducing and maintaining EoE remission, with a favorable safety profile. Clinicians should monitor histologic response, particularly during dose tapering, to optimize long-term management.

Data After Induction

After 12 weeks, data from 203 of 233 patients treated with 1 mg twice daily of BOTs were available. Clinical effectiveness was assessed through the DSQ score, which decreased from 28 ± 25 to 4 ± 10 ($P <$ .0001). The minimum clinically important difference (MCID) was −6.5 points, and a DSQ score <14 defined clinical inactivity. Patients with a DSQ score >14 dropped from 147 (63%) of 233 at baseline to 32 (16%) of 203 postinduction, with 171 (84%) of 203 achieving clinical remission; 136 (67%) of 203 had a DSQ score of 0. Analyzing the absolute change in DSQ, 145 (99%) of 174 patients experiencing clinical disease activity at baseline improved during induction period with a MCID of 16 points.

Table 1. Patient Demographics and Medical History

Demographic features	
Patients	233
Male	192 (82)
Age, y	37 ± 14
Body mass index, kg/m^2	23.1 ± 3.5
Smoking status	
Active smoking	25 (11)
Previous smoking	3 (1)
Allergic comorbidities	155 (67)
Other comorbidities	78 (35)
EoE features	
Age at diagnosis, y	32 ± 14
Disease duration, mo	59 ± 56
Clinical presentation	
Dysphagia	189 (81)
Odynophagia	42 (18)
Heartburn	95 (41)
Regurgitation	56 (24)
Chest pain	65 (28)
Food bolus impaction	165 (71)
Treatments	
PPI	
Previous treatment	193 (83)
Ongoing treatment	69 (30)
Clinical response	55 (24)
Maintained histological response	0 (0)
Dilatation	
Previous dilatation	24 (10)
Diet	
Ongoing	0 (0)
Previous diet	26 (10)

Values are n, mean ± SD, or n (%).
EoE, eosinophilic esophagitis; PPI, proton pump inhibitor.

Table 2. Baseline Disease Activity

Patients	233
Endoscopy	
EREFS	3 ± 2
Endoscopic features	
Exudates	103 (44)
Rings	150 (64)
Edema	129 (55)
Furrows	114 (49)
Stenosis	30 (13)
Eosinophilic Peak	
Distal esophagus, eos/hpf	31 ± 29
Mid esophagus, eos/hpf	28 ± 28
Proximal esophagus, eos/hpf	37 ± 35
Clinical Activity	
DSQ	28 ± 25
EoE-QoL-A	111 ± 36

Values are n, mean ± SD, or n (%).
DSQ, Dysphagia Symptom Questionnaire; EoE-QoL-A, Adult Eosinophilic Esophagitis Quality of Life questionnaire; EREFS, Endoscopic Reference Score; eos/hpf, eosinophils per high-power field.

Regarding HRQoL, the EoE-QoL-A score increased from 111 ± 36 to 140 ± 37 ($P < .0001$), indicating improvement, with 192 (95%) of 203 reporting better QoL.

Endoscopic findings improved postinduction, with the EREFS score decreasing from 3 ± 2 to 1 ± 1 ($P < .0001$). Complete endoscopic remission was achieved in 124 (61%) of 203, with significant reductions in all endoscopic features.

Histological analysis showed a reduction in eosinophilic peaks across all esophageal segments: distal (31 ± 29 to 3 ± 10; $P < .0001$), mid (28 ± 28 to 1 ± 4; $P < .0001$), and proximal (37 ± 35 to 2 ± 9; $P < .0001$) (Supplementary Figure 2). Deep histological remission (<6 eos/hpf in all segments) was reached by 170 (84%) of 203. Primary nonresponders (<15 eos/hpf) were 16 (8%) of 203, including 5 (2%) of 203 with no therapeutic benefit and 11 (5%) of 203 with partial improvement despite not achieving histological remission. Considering this subgroup, an analysis regarding potential predictive factors of nonresponse was performed: primary nonresponders were found to have a higher EREFS score at baseline compared with responders (4 ± 2 vs 3 ± 2; $P = .04$), as well as a longer disease duration (88 ± 119 months vs 47 ± 63 months; $P = .02$).

All findings are summarized in Table 3 and Supplementary Table 1.

Data on Maintenance Treatment

At 52 weeks, data were available for 86 of 203 patients. BOT maintenance dosages were 0.5 mg once daily in 11 (13%) of 86, 1 mg once daily in 68 (79%) of 86, and 1 mg twice daily in 7 (8%) of 86. No differences associated with the tapering dosages were found. The DSQ score significantly decreased from baseline (28 ± 25 to 3 ± 10; $P < .0001$), with 80 (93%) of 86 achieving inactive disease (DSQ <14). The MCID was 16 points. No statistical differences were found between DSQ scores at induction and maintenance (4 ± 10 vs 3 ± 10; $P = .44$) (Figure 1). The EoE-QoL-A score improved significantly from baseline (111 ± 36 to 141 ± 33; $P < .0001$). No differences were observed between scores at induction and maintenance (Supplementary Figure 3). The EREFS score also improved from baseline (3 ± 2 to 1 ± 1; $P < .0001$). Among 30 (13%) of 233 patients with strictures at baseline, only 1 (3%) of 30 had persistent esophageal narrowing. One new transitable stenosis occurred at 52 weeks, despite complete histological remission. No significant differences in EREFS scores between induction and maintenance were found (Table 4). Eosinophilic peaks remained significantly reduced at 52 weeks: distal (31 ± 29 to 6 ± 14; $P < .0001$), mid (28 ± 28 to 4 ± 12; $P < .0001$), and proximal (37 ± 35 to 1 ± 4; $P < .0001$) (Figure 2). Deep histological remission was maintained in 67 (78%) of 86, but 13 (15%) of 86 lost response with treatment tapering. All of them were treated with 1 mg of BOT once daily as

Table 3. Outcomes After 12-Week Induction (n = 203)

First Time Point Evaluation	T1	T0 vs T1	*P* Value
Endoscopy			
EREFS	1 ± 1	3 ± 2 vs 1 ± 1	<.0001[a]
Exudates	47 (23)	103 (44) vs 47 (23)	<.0001[a]
Rings	47 (23)	150 (64) vs 47 (23)	<.0001[a]
Edema	64 (32)	129 (55) vs 64 (32)	<.0001[a]
Furrows	40 (20)	114 (49) vs 40 (20)	<.0001[a]
Stenosis	9 (4)	30 (13) vs 9 (4)	<.0001[a]
Eosinophilic peak			
Distal esophagus	3 ± 10	31 ± 29 vs 3 ± 10	<.0001[a]
Mid esophagus	1 ± 4	28 ± 28 vs 1 ± 4	<.0001[a]
Proximal esophagus	2 ± 9	37 ± 35 vs 2 ± 9	<.0001[a]
Clinical activity			
DSQ	4 ± 10	28 ± 25 vs 4 ± 10	<.0001[a]
EoE-QoL-A	140 ± 37	111 ± 36 vs 140 ± 37	<.0001[a]

Values are n (%), or mean ± SD.
DSQ, Dysphagia Symptom Questionnaire; EoE-QoL-A, Adult Eosinophilic Esophagitis Quality of Life questionnaire; EREFS, Endoscopic Reference Score.
[a]Statistically significant data, cut-off $P < .05$.

maintenance dosage. Among them, 10 (77%) of 13 also showed worsening EREFS scores, though DSQ scores remained stable. Three patients were classified as secondary nonresponders. A slight increase in eos/hpf was observed at 52 weeks compared with 12 weeks in distal (3 ± 10 vs 6 ± 14; $P = .04$) and mid (1 ± 4 vs 4 ± 12; $P = .002$) esophagus. As well as for primary nonresponders, a specific subanalysis showed that secondary nonresponders presented a higher EREFS score at baseline compared with responders (5 ± 3 vs 3 ± 2; $P = .003$).

All findings for the T2 time point are summarized in Table 4 and Supplementary Table 2.

Safety Profile

BOTs were well tolerated, with only mild side effects related to drug assumption reported in 28 (12%) of 233 patients. The most common were oral symptoms, including candidiasis, oral ulcers, and mouth sores (n = 20 of 233 [9%]). Three (15%) of 20 patients discontinued BOTs before 52 weeks due to candidiasis recurrence. Nonspecific corticosteroid-related symptoms, such as bloating, epigastric pain, weight gain, and altered bowel movements, were reported by 6 (3%) of 233, leading to treatment discontinuation in 4 (2%) of 233. Additionally, de novo chronic cough without candidiasis was observed on 2 (1%) of 28 but did not require treatment cessation.

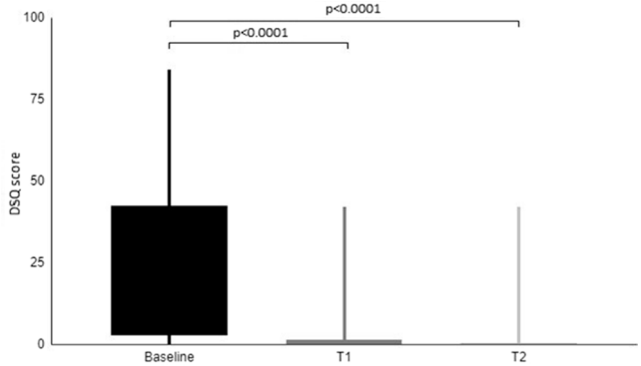

Figure 1. Dysphagia Symptom Questionnaire score changes over time.

Discussion

A novel formulation of topical budesonide has recently been introduced in the European market, demonstrating efficacy and safety in RCTs.[34,37] However, real-world data are essential to assess its effectiveness in routine practice. To our knowledge, this study is the first prospective, multicenter trial evaluating BOT therapy for EoE in a real-life setting.

Among 273 patients, 233 were enrolled, and 203 completed the 12-week assessment. After 12 weeks of induction therapy, clinical activity and QoL significantly improved, with DSQ score reduction and increased EoE-QoL-A values. Endoscopic remission (EREFS <2) was achieved in 61%, while 84% attained deep histological remission (<6 eos/hpf) and 8% had significant histological remission (6–15 eos/hpf). All patients in histological remission also showed clinical improvement (DSQ <14 in 95%). Over 1 year, clinical effectiveness was maintained, with persistent DSQ and QoL improvements. Endoscopic remission remained stable, but 78% stayed in deep remission, while 6% (n = 13 of 203) lost response, mainly after dose tapering. Additionally, 8% (n = 7 of 86) had partial histological response (6–15 eos/hpf). A mean eos/hpf increase in distal and mid

Table 4. Outcomes after 52-Week Maintenance (n = 86)

Second Time Point Evaluation	T2	T0 vs T2	*P*	T1 vs T2	*P*
Endoscopy					
EREFS	1 ± 1	3 ± 2 vs 1 ± 1	<.0001[a]	1 ± 1 vs 1 ± 1	1.0
Exudates	15 (17)	103 (44) vs 15 (17)	<.0001[a]	47 (23) vs 15 (17)	.4
Rings	25 (29)	150 (64) vs 25 (29)	<.0001[a]	47 (23) vs 25 (29)	.4
Edema	31 (36)	129 (55) vs 31 (36)	<.0001[a]	64 (32) vs 31 (36)	.5
Furrows	18 (21)	114 (49) vs 18 (21)	<.0001[a]	40 (20) vs 18 (21)	.9
Stenosis	2 (2)	30 (13) vs 2 (2)	<.0001[a]	9 (4) vs 2 (2)	.6
Eosinophilic peak					
Distal esophagus	6 ± 14	31 ± 29 vs 6 ± 14	<.0001[a]	3 ± 10 vs 6 ± 14	.04[a]
Mid esophagus	4 ± 12	28 ± 28 vs 4 ± 12	<.0001[a]	1 ± 4 vs 4 ± 12	.002[a]
Proximal esophagus	1 ± 4	37 ± 35 vs 1 ± 4	<.0001[a]	2 ± 9 vs 1 ± 4	.32
Clinical activity					
DSQ	3 ± 10	28 ± 25 vs 3 ± 10	<.0001[a]	4 ± 10 vs 3 ± 10	.44
EoE-QoL-A	140 ± 36	111 ± 36 vs 141 ± 33	<.0001[a]	140 ± 37 vs 141± 33	.82

Values are n (%), or mean ± SD.
DSQ, Dysphagia Symptom Questionnaire; EoE-QoL-A, Adult Eosinophilic Esophagitis Quality of Life questionnaire; EREFS, Endoscopic Reference Score.
[a]Statistically significant data, cut-off $P < .05$.

esophagus was noted at 52 weeks. BOTs were well tolerated, with mild side effects in 12%, mainly oral/esophageal candidiasis (9%). Treatment discontinuation due to adverse events occurred in 3% (n = 7 of 233).

The efficacy and effectiveness of BOTs has been consistently demonstrated in published studies. In 2019, Lucendo et al[33] conducted a double-blind, parallel study in 88 adults with active EoE, comparing BOTs (1 mg twice daily) to placebo. At 6 weeks, 58% of BOT-treated patients achieved complete clinic-histological remission, and 93% met the secondary endpoint of histologic remission. By 12 weeks, 85% of patients achieved complete remission.[33] Consistently, our study found an 84% rate of deep histological remission and an 84% rate of clinical remission following 12 weeks of induction therapy, reinforcing the real-world effectiveness of BOTs.

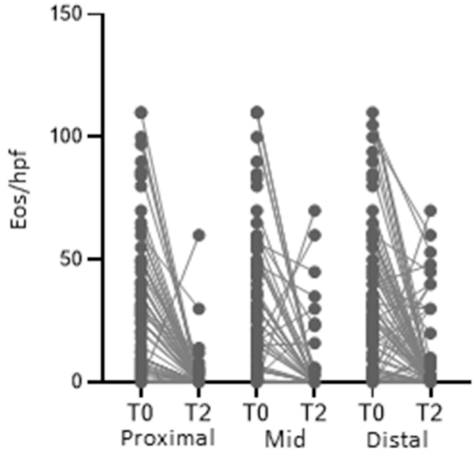

Figure 2. Comparison of eosinophilic peaks between baseline (T0) and after maintenance treatment (T2).

Subsequent phase 3 trial data confirmed that after 48 weeks of BOT therapy, 73.5% of patients on 0.5 mg twice daily and 75% on 1.0 mg twice daily achieved sustained clinical and histological remission.[32] Consistent with these findings and other published data, our study observed a 78% clinical response rate after 52 weeks of therapy. However, 15% (n = 13 of 86) of patients who had achieved histological remission after induction experienced loss of response at 52 weeks, with an EREFS score increase in 77% (n = 10 of 13), though clinical response was maintained. Additionally, eos/hpf levels increased in the distal and mid esophagus at 52 weeks, indicating a potential decline in long-term effectiveness.

Additionally, there was an overall increase in eos/hpf in the distal and mid esophagus at 52 weeks compared with 12 weeks, suggesting a potential reduction in long-term effectiveness. These findings emphasize the importance of close follow-up. A similar trend was observed in the phase 3 extension study of budesonide oral suspension 2.0 mg twice daily, where 25% of patients who initially responded after 12 weeks experienced relapse despite continued treatment for 36 additional weeks.[37] Likewise, for BOTs, approximately 25% of patients in remission after a 6-week induction phase lost remission after an additional 48 weeks of treatment.[32] These findings suggest that further studies are needed to evaluate the long-term maintenance of effectiveness in patients treated with topical steroids.

According to the inclusion criteria, concomitant PPI therapy was permitted if stable for at least 8 weeks before initiating BOT treatment. In our cohort, 30% of patients were on stable PPI therapy at enrollment. Among these, all had histological inflammation and 76% had persistent symptoms at study inclusion. This aligns with findings from other real-world studies, in which PPI therapy is

frequently continued despite the lack of histological remission when initiating a second-line treatment. The impact of concurrent PPI therapy on BOT effectiveness deserves special consideration. While our data showed a nonsignificant trend (n = 5 of 18 of primary nonresponders were on a PPI, which corresponds to the 30% of the subpopulation considered; n = 4 of 13 of secondary nonresponders were on a PPI, which corresponds to the 30% of the subpopulation considered) toward lower response rates in patients receiving PPI cotherapy (which is the same rate of the overall population), the clinical implications of this observation remain uncertain. Potential explanations include selection bias (patients on PPI therapy may have more refractory disease) or pharmacokinetic interactions affecting budesonide bioavailability. Conversely, some studies have suggested potential synergistic effects between PPIs and topical corticosteroids, possibly through complementary anti-inflammatory mechanisms. Our findings suggest that BOT remains effective in most PPI nonresponders, but further research specifically designed to assess optimal combination strategies is warranted.

The EREFS score significantly improved from baseline after the induction phase, with results remaining stable over 1 year and reaching a low mean value (EREFS: 1). Notably, the prevalence of esophageal strictures decreased from 13% at baseline to 3% at study completion. Literature supports that anti-inflammatory therapies, including TCs, improve fibrotic features, as assessed through histology, EREFS scoring, and esophageal distensibility (EndoFLIP).[35,36,38] In 2021, Navarro et al[38] demonstrated that TCs reduced strictures from 42% to 3%, as well as other parameters of fibrosis such as rings. Further EndoFLIP analysis in 6 TC responders showed an increase in esophageal diameter across all incremental volumes, with significant compliance improvements at 40 mL distension.[38] The significance of these findings lies behind the possibility to reverse fibrosis, an aim pursued by all therapies. By definition, fibrosis stands together with the concept of irreversibility. Considering the results of our study as well as the available literature, it seems too early to say whether the improvements in the EREFS subscores of fibrosis genuinely reflect its regression. Likely, strictures and rings possess an inflammatory component that contributes to their structure and caliber, making them responsive to anti-inflammatory treatment. To gather meaningful data on fibrosis regression, it will be necessary to assess whether maintenance therapy, following histological remission, can further improve fibrotic features. Obviously, if these findings are confirmed by future studies, the indication for maintenance therapy will be further strengthened, with the potential to alter the natural course of this disease.

Regarding safety, BOTs were well tolerated, with mild side effects reported in 12% of patients, primarily related to drug administration. The most frequently reported AE was candidiasis (9%), followed by various nonspecific gastrointestinal symptoms.

The frequency of AEs in our study aligns with findings from the phase 3 trial, where clinically manifest candidiasis was suspected in 16.2% of patients in the BOT 0.5 mg group and 11.8% in the BOT 1.0 mg group.[32] However, unlike the phase 3 study, in which no patients discontinued treatment due to AEs, in our study, 1% (n = 3 of 233) of patients discontinued due to refractory candidiasis despite antifungal therapy, and 2% (n = 4 of 233) discontinued due to new-onset gastrointestinal symptoms potentially related to BOT use.

This study is notable as the first prospective trial specifically designed to evaluate the effectiveness of BOTs in a real-life setting. Additionally, the study aimed not only to assess effectiveness following the induction phase, but also to evaluate its maintenance benefit over the course of 1 year. On the other hand, our study has some limitations. First, patients were not stratified based on their response to previous therapies, particularly PPIs. Second, a significant proportion of patients were unable to complete the study with the 52-week evaluation. Another limitation is that the cohort consisted primarily of patients from referral hospitals. A notable limitation of our study is that BOT is not universally available worldwide. While other formulations deliver topical budesonide to the esophageal mucosa, such as budesonide oral suspensions, caution should be exercised when generalizing our findings[23]

In conclusion, our real-world data on the effectiveness and safety of BOTs aligns well with the existing literature. Treatment with BOTs effectively induced and maintained clinical histologic remission in the majority of EoE patients. The safety profile of this drug was favorable, with AEs reported by only a minority of patients.

Supplementary Material

NOTE: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2025.08.033.

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Conflicts of interest

These authors disclose the following: Matteo Ghisa has served for Pfizer, Reckitt Benckiser, SILA, Zeta Farmaceutici, and Unifarco. Roberto Penagini has served as a speaker for Dr. Falk Pharma and Sanofi. Pierfrancesco Visaggi has served as a speaker for Dr. Falk, JB Pharmaceuticals, Malesci, and Sanofi. Nicola de Bortoli has received lecture fees from Malesci, Reckitt Benckiser, Dr. Falk, and Sanofi. Edoardo Vespa has served as a consultant for Apollo Therapeutics, Aurora Biofarma, Dr. Falk Pharma, and Sanofi; and as a speaker for Recordati and Sanofi. Marco Caminati has received speaker fees and research grants from AstraZeneca, GSK, Pfizer, and Sanofi. Elisa Marabotto has received support from Alfasigma and Dr. Falk. Pasta Andrea as received support from Fenix Pharma. Edoardo Vincenzo Savarino has served as a speaker for AbbVie, Abivax, Agave, AGPharma, Alfasigma, Apoteca, Biosline, CaDiGroup, Celltrion, Dr. Falk, EG Stada Group, Fenix Pharma, Galapagos, Johnson & Johnson, JB Pharmaceuticals, Innovamedica/Adacyte, Eli Lilly, Malesci, Mayoly Biohealth, Montefarco, Novartis, Omega Pharma, Pfizer, Rafa, Reckitt Benckiser, Sandoz, Sanofi/Regeneron, SILA, Sofar, Takeda, Tillots, and Unifarco; has served as a consultant for AbbVie, Agave, Alfasigma, Biogen, Bristol-Myers Squibb, Celltrion, Dr. Falk, Eli Lilly, Fenix Pharma, Ferring, Giuliani, Grünenthal, Johnson & Johnson, JB Pharmaceuticals, Merck & Co., Nestlé, Pfizer, Reckitt Benckiser, Sanofi/Regeneron, SILA, Sofar, Takeda, and Unifarco; has received research support from Bonollo, Difass, Pfizer, Reckitt Benckiser, Sanofi/Regeneron, SILA, Sofar, Unifarco, and Zeta Farmaceutici. The remaining authors disclose no conflicts.

Data Availability

De-identified individual participant data, including study protocol and statistical analysis plan, will be made available upon reasonable request.