Triple Therapy Optimises COPD Outcomes at ATS 2026

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Managing chronic obstructive pulmonary disease (COPD) and asthma-COPD overlap (ACO) often presents a clinical challenge, particularly in patients with persistent symptoms despite dual bronchodilator therapy. The American Thoracic Society (ATS) 2026 meeting underscored the role of triple therapy, specifically fixed-dose combinations of inhaled corticosteroids (ICS), long-acting beta-agonists (LABA), and long-acting muscarinic antagonists (LAMA), in optimising patient outcomes.

KEY TAKEAWAYS

- The Pivot: Fixed-dose triple therapy is increasingly the standard for symptomatic COPD patients with a history of exacerbations.
- The Data: Triple therapy consistently demonstrates superior improvements in forced expiratory volume in 1 second (FEV1) and reduction in moderate-to-severe exacerbations compared to dual therapy.
- The Action: Clinicians should consider initiating fixed-dose triple therapy in COPD patients with persistent symptoms, an FEV1 less than 50% predicted, and a history of exacerbations, particularly those with elevated eosinophil counts.

The management of obstructive lung diseases, including chronic obstructive pulmonary disease (COPD) and asthma-COPD overlap (ACO), necessitates a stratified approach to pharmacotherapy. While dual bronchodilation with a long-acting beta-agonist (LABA) and a long-acting muscarinic antagonist (LAMA) remains a cornerstone for many patients, a significant subset continues to experience symptomatic burden and recurrent exacerbations.1 The ATS 2026 sessions focused on the evidence supporting the escalation to triple therapy, defined as the combination of an inhaled corticosteroid (ICS), a LABA, and a LAMA, particularly in patients with specific clinical phenotypes.

The rationale for triple therapy stems from the recognition that a proportion of COPD patients exhibit features responsive to corticosteroids, often indicated by a history of asthma, elevated blood eosinophil counts, or frequent exacerbations despite optimal bronchodilator use.2 The addition of an ICS to dual bronchodilation aims to address airway inflammation, thereby reducing exacerbation rates and improving lung function.3 The underlying pathophysiology of COPD involves chronic inflammation, which contributes to airflow limitation and disease progression. While bronchodilators primarily target smooth muscle relaxation, ICS addresses the inflammatory component, particularly in patients with an eosinophilic phenotype. This targeted approach is crucial given the heterogeneity of COPD and the varying contributions of different inflammatory pathways.

Clinical Evidence for Triple Therapy

Multiple large-scale, randomised controlled trials have evaluated the efficacy and safety of fixed-dose triple therapy compared to dual bronchodilator or ICS/LABA combinations. These studies consistently demonstrated that triple therapy provides superior improvements in lung function, as measured by forced expiratory volume in 1 second (FEV1), and a reduction in the rate of moderate-to-severe COPD exacerbations.4 For instance, a meta-analysis of four pivotal trials (N=15,000+ patients) reported that triple therapy reduced the annualised rate of moderate-to-severe exacerbations by 25% (Rate Ratio [RR] 0.75, 95% CI 0.70-0.80; p<0.001) compared to LABA/LAMA.5 Furthermore, the reduction in severe exacerbations requiring hospitalisation was also statistically significant, with an RR of 0.78 (95% CI 0.70-0.87; p<0.001).5 These trials typically enrolled patients with moderate-to-severe COPD, a history of exacerbations, and often a specific eosinophilic phenotype, ensuring the study population was representative of those most likely to benefit from ICS.

Improvements in FEV1 were also consistently observed, with mean differences typically ranging from 50 mL to 100 mL compared to dual bronchodilator therapy, a change considered clinically meaningful in the context of COPD progression.6 Patient-reported outcomes, including health-related quality of life scores (e.g., St. George's Respiratory Questionnaire, SGRQ), also showed statistically significant improvements with triple therapy.7 These improvements reflect a reduction in symptoms such as dyspnea and cough, leading to an enhanced daily quality of life for patients.

The identification of patients most likely to benefit from ICS remains a critical aspect of treatment selection. Elevated blood eosinophil counts have emerged as a biomarker predictive of ICS responsiveness.8 Studies presented at ATS 2026 reinforced that patients with baseline blood eosinophil counts of ≥100 cells/μL or ≥300 cells/μL derive greater benefit from the ICS component of triple therapy in terms of exacerbation reduction.9 Conversely, patients with very low eosinophil counts (e.g., <100 cells/μL) may experience less benefit from ICS and potentially increased risk of pneumonia without a commensurate reduction in exacerbations.10 This highlights the importance of phenotyping patients to optimise treatment efficacy and minimise potential adverse effects.

Safety profiles of fixed-dose triple therapies were generally consistent with the known effects of their individual components. The most frequently reported adverse events included nasopharyngitis, headache, and oral candidiasis.11 A slight increase in the incidence of pneumonia was observed with ICS-containing regimens, particularly in patients with lower baseline eosinophil counts, reinforcing the need for careful patient selection.12 However, this risk was often outweighed by the benefits in exacerbation reduction in appropriate patient populations.13

Limitations of current evidence include the generalisability to all COPD phenotypes, particularly those with rare comorbidities or very severe disease not typically enrolled in large trials. Long-term data beyond 12 months for some fixed-dose combinations are also still accumulating. Future research is expected to further refine patient selection strategies, potentially incorporating additional biomarkers or genetic profiling to personalise triple therapy initiation and de-escalation. The impact of triple therapy on cardiovascular outcomes, a significant comorbidity in COPD, also warrants further investigation.

For deeper insights into the diagnosis and comprehensive management of COPD and related respiratory diseases, readers may find the Oxford Handbook of Respiratory Medicine an excellent resource.

CLINICAL IMPLICATIONS

The consistent data presented at ATS 2026 regarding fixed-dose triple therapy for obstructive lung disease should prompt a re-evaluation of current prescribing patterns. For patients with COPD who continue to experience exacerbations despite dual bronchodilator therapy, particularly those with an eosinophilic phenotype, the evidence for ICS/LABA/LAMA is now robust enough to warrant its consideration as a primary escalation strategy. This moves beyond the historical reluctance to add ICS due to pneumonia concerns, provided patient selection is guided by clinical history and eosinophil counts. The convenience of single-inhaler triple therapy also offers a practical advantage, potentially improving adherence compared to multiple devices.
Pharmaceutical companies, particularly those with established fixed-dose triple therapy products such as GlaxoSmithKline's Trelegy Ellipta or AstraZeneca's Breztri Aerosphere, will likely see continued market growth. The emphasis on tailored approaches, however, means that a 'one-size-fits-all' marketing strategy will be less effective. Instead, educational initiatives focusing on biomarker-guided therapy and the nuances of patient selection will be critical. This also places a greater onus on diagnostic laboratories to provide timely and accurate eosinophil counts to support clinical decision-making.
For patients, the implications are significant. A more targeted approach to triple therapy means fewer exacerbations, improved lung function, and a better quality of life. The reduction in hospitalisations for severe exacerbations is a tangible benefit, not just for the individual but also for healthcare systems grappling with the economic burden of COPD. However, clinicians must remain vigilant regarding the potential for ICS-related side effects, particularly pneumonia, and engage in shared decision-making with patients to balance benefits and risks. The goal is not merely to add another drug, but to ensure the right drug combination reaches the right patient.

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