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Review Article

Vilanterol vs formoterol in obstructive airway diseases: A comprehensive review of efficacy, safety, and clinical advantages in light of Global Initiative for Asthma 2024 and Global Initiative for Chronic Obstructive Lung Disease 2024 guidelines

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ABSTRACT

This comprehensive review evaluates the comparative efficacy, safety, and clinical advantages of vilanterol versus formoterol in the management of obstructive airway diseases, with a specific focus on the latest Global Initiative for Asthma (GINA) 2024 and Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2024 guideline recommendations. Vilanterol, a novel long-acting β2-agonist (LABA), demonstrates a 24-hour duration of action, allowing for once-daily dosing, compared to formoterol's twice-daily requirement. Clinical trials in both asthma and chronic obstructive pulmonary disease (COPD) have shown vilanterol-containing combinations to be at least as effective as formoterol-based treatments in improving lung function, symptom control, and quality of life. However, the GINA 2024 guidelines emphasize formoterol's role in as-needed and maintenance and reliever therapy (MART) approaches for asthma management. In COPD, vilanterol aligns well with GOLD 2024 recommendations, particularly in fixed-dose combinations. Safety analyses indicate a favorable profile for vilanterol, even in high-risk populations. The once-daily dosing of vilanterol offers potential improvements in patient adherence and satisfaction, especially relevant in COPD management. While direct cost comparisons are limited, improved clinical outcomes suggest potential cost-effectiveness benefits. This review concludes that while vilanterol presents several advantages, particularly in COPD management and once-daily regimens, the choice between vilanterol and formoterol should be individualized based on patient characteristics, disease features, and current guideline recommendations.

Keywords: Vilanterol, Formoterol, Asthma, COPD, GINA 2024, GOLD 2024

INTRODUCTION

Obstructive airway diseases, primarily asthma and chronic obstructive pulmonary disease (COPD), remain significant global health concerns. Long-acting β2-agonists (LABAs) have become a cornerstone in the management of these conditions, often used in combination with inhaled corticosteroids (ICS) or long-acting muscarinic antagonists (LAMA). Among the LABAs, vilanterol and formoterol are widely used. This review aims to compare vilanterol and formoterol in various aspects of obstructive airway disease management, with particular attention to the latest *Global Initiative for Asthma (GINA)* 2024 and *Global Initiative for Chronic Obstructive Lung Disease (GOLD)* 2024 guidelines.

Current guideline recommendations

GINA 2024 Guidelines for Asthma Management.[1] GINA 2024 guidelines emphasize a significant shift in asthma management. For adults and adolescents, GINA now recommends:

- As-needed low-dose ICS-formoterol as the preferred reliever across all asthma severities.
- Regular low-dose ICS-formoterol maintenance and reliever therapy (MART) as the preferred Step 3–5 controller option.

These recommendations highlight the importance of formoterol's rapid onset of action in the context of as-needed and MART approaches. However, the guidelines also acknowledge the role of other LABA-containing combinations, including those with vilanterol, as alternative controller options.

GOLD 2024 Guidelines for COPD Management.[2] The GOLD 2024 report maintains the importance of LABAs in COPD management:

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- LABAs are recommended as initial pharmacological treatment for most COPD patients, either alone or in combination with LAMA.
- For patients with exacerbations, LABA-LAMA or LABA-ICS combinations are recommended based on blood eosinophil counts and exacerbation history.

The GOLD guidelines do not differentiate between specific LABAs but emphasize the importance of individualized treatment based on patient characteristics and preferences.

Pharmacological properties

Vilanterol trifenatate is a novel LABA with a rapid onset and prolonged duration of action. It demonstrates high selectivity and potency for the β2-adrenoreceptor, with minimal activity at β1 and β3 receptors.[3] The molecular structure of vilanterol allows for a longer residence time at the β2-receptor, contributing to its extended duration of action.[4]

Formoterol, on the other hand, is a well-established LABA with a rapid onset of action but a shorter duration compared to vilanterol. While both drugs are effective bronchodilators, the pharmacological profile of vilanterol offers some distinct advantages:

***Duration of action*:** Vilanterol has demonstrated a 24-hour duration of bronchodilation, allowing for once-daily dosing.[5,6] This extended action is a significant improvement over formoterol, which typically requires twice-daily dosing. The longer duration of vilanterol may contribute to improved adherence and potentially better symptom control throughout the day and night.[7,8]

***Onset of action*:** While both vilanterol and formoterol have a rapid onset of action, some studies suggest that vilanterol may have a faster onset in certain patient populations.[3] However, it's important to note that the GINA 2024 guidelines specifically recommend formoterol for its rapid onset in as-needed and MART approaches.[1]

***Potency*:** In vitro studies have shown that vilanterol exhibits greater potency at the β2-receptor compared to formoterol.[3] This increased potency may translate to greater efficacy at lower doses, potentially reducing the risk of dose-related adverse effects.

Clinical efficacy

Asthma:

Several clinical trials have compared the efficacy of vilanterol-containing combinations to formoterol-containing combinations in asthma management:

- *Symptom control*: A retrospective matched cohort study by Averell *et al*. (2022) compared the effectiveness of fluticasone furoate/vilanterol (FF/VI) to budesonide/formoterol (BUD/FOR) in real-world asthma management. The study found that patients using FF/VI had significantly better symptom control and lower short-acting β2-agonist (SABA) use compared to those using BUD/FOR.[9] This suggests that the once-daily dosing of FF/VI may provide more consistent symptom relief throughout the day.
- *Lung function*: In a randomized crossover trial, Furuhashi *et al*. (2019) compared once-daily FF/VI to twice-daily BUD/FOR in patients with controlled stable asthma. The study demonstrated that FF/VI provided similar improvements in lung function (measured by forced expiratory volume in 1 second, FEV1) to BUD/FOR, but with the advantage of once-daily dosing.[7]
- *Quality of life*: Bernstein *et al*. (2018) conducted a study comparing FF/VI to fluticasone propionate/salmeterol in patients with well-controlled asthma. While both treatments maintained asthma control, patients reported higher satisfaction with the once-daily FF/VI regimen, which could potentially lead to improved adherence and long-term outcomes.[8]
- *Exacerbation prevention*: The CAPTAIN study, while not directly comparing vilanterol to formoterol, demonstrated the efficacy of FF/VI in reducing severe exacerbations in patients with uncontrolled asthma.[10] The once-daily dosing of FF/VI may contribute to better adherence and, consequently, improved exacerbation prevention compared to twice-daily formoterol-containing regimens.

COPD:

In COPD management, vilanterol has shown promising results in various clinical endpoints, aligning with the GOLD 2024 recommendations:

- *Lung function*: The early maximization of bronchodilation for improving COPD stability (EMAX) trial, while not directly comparing vilanterol to formoterol, demonstrated the efficacy of umeclidinium/vilanterol in improving lung function compared to monotherapy bronchodilators in symptomatic COPD patients.[11] This supports the GOLD 2024 recommendation for LABA–LAMA combinations in certain patient groups.[2]
- *Exacerbation reduction*: Dransfield *et al*. (2013) conducted two replicate double-blind, parallel-group, randomized controlled trials comparing FF/VI to vilanterol alone in COPD patients. The study found that FF/VI significantly reduced the rate of moderate and severe exacerbations compared to vilanterol monotherapy, highlighting the efficacy of vilanterol-containing combinations

in exacerbation prevention.[12] This aligns with the GOLD 2024 recommendations for using LABA–ICS combinations in patients with high exacerbation risk and elevated blood eosinophil counts.[2]

- *Mortality*: The SUMMIT trial, a large-scale study involving COPD patients with heightened cardiovascular risk, evaluated the effect of FF/VI on all-cause mortality. While the primary endpoint was not met, the study provided valuable data on the safety and potential benefits of FF/VI in a high-risk COPD population.[13,14]
- *Real-world effectiveness*: The Salford Lung Study, a groundbreaking real-world effectiveness trial, compared FF/VI to usual care in COPD patients. The study found that FF/VI was associated with a significantly lower rate of moderate or severe exacerbations compared to usual care, which often included formoterol-containing combinations.[15] This real-world evidence supports the superiority of vilanterol-containing regimens in everyday clinical practice and aligns with the GOLD 2024 emphasis on individualizing treatment based on patient characteristics and preferences.[2]

Safety profile

The safety profile of vilanterol has been extensively studied in both asthma and COPD populations, addressing concerns highlighted in both GINA 2024 and GOLD 2024 guidelines:

***Cardiovascular safety*:** Given the potential for β2-agonists to affect heart rate and blood pressure, the cardiovascular safety of vilanterol has been a focus of research. The SUMMIT trial, which included COPD patients with cardiovascular risk factors, did not show an increased risk of cardiovascular events with FF/VI compared to placebo.[13] This provides reassurance regarding the cardiovascular safety of vilanterol, even in high-risk populations, aligning with the GOLD 2024 recommendations for careful assessment of comorbidities in COPD management.[2]

***Pneumonia risk*:** In COPD patients, there has been concern about the potential increased risk of pneumonia with ICS/LABA combinations. Crim *et al*. (2015) analyzed pneumonia risk in two replicate trials comparing FF/VI to vilanterol alone in COPD patients. While there was a numerical increase in pneumonia events with FF/VI, the overall incidence was low, and the benefit–risk profile remained favorable.[16] A subsequent analysis of pneumonia risk in the SUMMIT trial similarly found a low overall incidence of pneumonia events.[17] These findings are relevant to the GOLD 2024 recommendations, which acknowledge the potential pneumonia risk with ICS use but maintain the role of ICS/LABA combinations in appropriate patient groups.[2]

***Age-related safety*:** Hanania *et al*. (2021) conducted analyses of five randomized clinical trials to evaluate the effect of age on the efficacy and safety of FF/VI and umeclidinium/vilanterol in COPD patients. The study found that the safety profile of vilanterol-containing regimens was consistent across different age groups, suggesting that vilanterol is well-tolerated in both younger and older patients.[18]

***Long-term safety*:** Busse *et al*. (2013) conducted a 52-week study evaluating the safety and tolerability of FF/VI in asthma patients. The study found that FF/VI was well-tolerated over the long term, with no new safety signals identified.[19] This long-term safety data are particularly important given the chronic nature of asthma and COPD management, as emphasized in both GINA 2024 and GOLD 2024 guidelines.[1,2]

Patient adherence and preference

The once-daily dosing of vilanterol-containing combinations offers a significant advantage over twice-daily formoterol regimens in terms of patient adherence and preference, an important consideration in both GINA 2024 and GOLD 2024 guidelines:

***Simplified regimen*:** The ability to use a once-daily inhaler can significantly simplify treatment regimens, potentially leading to improved adherence. This is particularly important in COPD patients, who often have multiple comorbidities and complex medication regimens.[4]

***Patient satisfaction*:** Studies comparing once-daily FF/VI to twice-daily ICS/LABA combinations have consistently shown higher patient satisfaction with the once-daily regimen.[8,20] This increased satisfaction may translate to better long-term adherence and outcomes, aligning with the patient-centered approach advocated in both GINA 2024 and GOLD 2024 guidelines.[1,2]

***Real-world adherence*:** A real-world study conducted in India by Prabhudesai *et al*. (2023) evaluated the use trends and characteristics of FF/VI in patients with obstructive airway disease. The study found high persistence rates with FF/VI treatment, suggesting good real-world adherence to the once-daily regimen.[21] This real-world evidence supports the potential adherence benefits of vilanterol-containing regimens.

Cost-effectiveness

While direct cost comparisons between vilanterol and formoterol-containing regimens are limited, the potential for improved adherence and reduced exacerbation rates with vilanterol may contribute to the overall cost-effectiveness:

***Reduced healthcare utilization*:** The Salford Lung Study demonstrated a reduction in moderate to severe exacerbations with FF/VI compared to usual care in COPD patients.[15] Given the significant healthcare costs associated with COPD exacerbations, this reduction could translate to substantial cost savings, aligning with the GOLD 2024 emphasis on exacerbation prevention.[2]

***Improved productivity*:** The once-daily dosing of vilanterol-containing regimens may lead to improved symptom control throughout the day, potentially resulting in better work productivity and reduced absenteeism. While not directly measured in most clinical trials, this could contribute to the overall economic benefit of vilanterol-based treatments.

Future directions

As our understanding of obstructive airway diseases evolves, so too does the role of LABAs like vilanterol, with several areas of focus aligned with GINA 2024 and GOLD 2024 guidelines:

***Personalized medicine*:** Both GINA 2024 and GOLD 2024 emphasize the importance of individualizing treatment based on patient characteristics and preferences.[1,2] Future research may focus on identifying specific patient subgroups that derive the greatest benefit from vilanterol-containing regimens. For example, studies have begun to explore the role of blood eosinophil counts in predicting response to ICS/LABA combinations in COPD.[22]

***Triple therapy*:** The development of single-inhaler triple therapy combinations containing vilanterol (such as fluticasone furoate/umeclidinium/vilanterol) represents an exciting area of research, particularly relevant to the GOLD 2024 recommendations for certain COPD patient groups.[2] Early studies have shown promising results in terms of exacerbation reduction and potential mortality benefits in COPD patients.[23,24]

***Comparative effectiveness*:** While this review has focused on the comparison between vilanterol and formoterol, future studies may provide more direct head-to-head comparisons with other LABAs or explore the relative efficacy of different LABA/LAMA combinations.[25,26] Such studies will be crucial in refining treatment algorithms in line with GINA and GOLD guidelines.

***Role in asthma-COPD overlap*:** Both GINA 2024 and GOLD 2024 acknowledge the challenges in managing patients with features of both asthma and COPD.[1,2] Future research may explore the specific benefits of vilanterol-containing regimens in this patient population.

CONCLUSION

In light of the GINA 2024 and GOLD 2024 guidelines, the evidence reviewed suggests that vilanterol offers several advantages over formoterol in the management of obstructive airway diseases, particularly in COPD. Its once-daily dosing, prolonged duration of action, and favorable efficacy and safety profile make it an attractive option for COPD management, aligning well with the GOLD 2024 recommendations for individualized treatment and the use of LABA-containing combinations.

The choice between vilanterol and formoterol should be individualized based on patient characteristics, preferences, specific disease features, and treatment goals, as emphasized by both GINA and GOLD guidelines. While vilanterol demonstrates advantages in many aspects, particularly in COPD management and once-daily regimens, formoterol remains an effective and valuable treatment option, especially in the context of current asthma management recommendations.

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