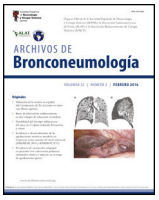
Archivos de Bronconeumología xxx (xxxx) xxx–xxx

Sociedad Española de Neumología y Cirugía Torácica SEPAR

ARCHIVOS DE
Bronconeumología

www.archbronconeumol.org



Editorial

The COPD Kaleidoscope: Breaking Bad Dogmatic Recommendations

Over the past decades, the pharmacological management of chronic obstructive pulmonary disease (COPD) has undergone significant advancements. Initially, treatment decisions were predominantly guided by patients' respiratory function.[1] However, the parameters influencing optimal therapeutic choices have expanded considerably.[2] This complexity arises from the continuous development of new therapeutic options and an enhanced understanding of the diverse clinical phenotypes of COPD and their prognostic implications. Consequently, clinicians must now consider a myriad of disease-specific factors when tailoring treatment plans for individual patients, posing a significant challenge in real-world clinical practice.

Current guidelines for COPD management primarily rely on therapeutic algorithms derived from clinical trials that assess the efficacy and safety of treatments under controlled conditions. This evidence-based approach serves as a cornerstone for developing standardized recommendations, offering clear directives on when and how to use specific therapies. However, it is well recognized that clinical trials often fail to fully represent the complexity of real-world COPD. Studies reveal that the representativeness of real-world patients in clinical trials remains alarmingly low.[3] This gap can be attributed to two primary factors. First, clinical trials are designed to meet regulatory requirements for drug approval, which may not align with evaluating real-world effectiveness. Second, strict eligibility criteria in these trials aim to isolate therapeutic effects within narrowly defined clinical contexts.[4] As a result, the application of trial-based guidelines frequently falls short in addressing the nuanced realities faced by practicing clinicians.[5,6] In routine clinical practice, numerous factors influencing pharmacological prescriptions are seldom addressed in guideline documents. These include comorbidities, patients' social circumstances, previous treatment experiences, and the rate of disease progression, to mention a few. Faced with these complexities, clinicians often find themselves compelled to intensify treatment in the absence of definitive guidance, hoping to elicit a favorable response.

Given these considerations, rigid, dogmatic guidelines may not adequately address the needs of real-world COPD patients. Instead, a more individualized approach—considering a range of patient-specific variables—may optimize therapeutic outcomes while minimizing polypharmacy. Among these variables, four

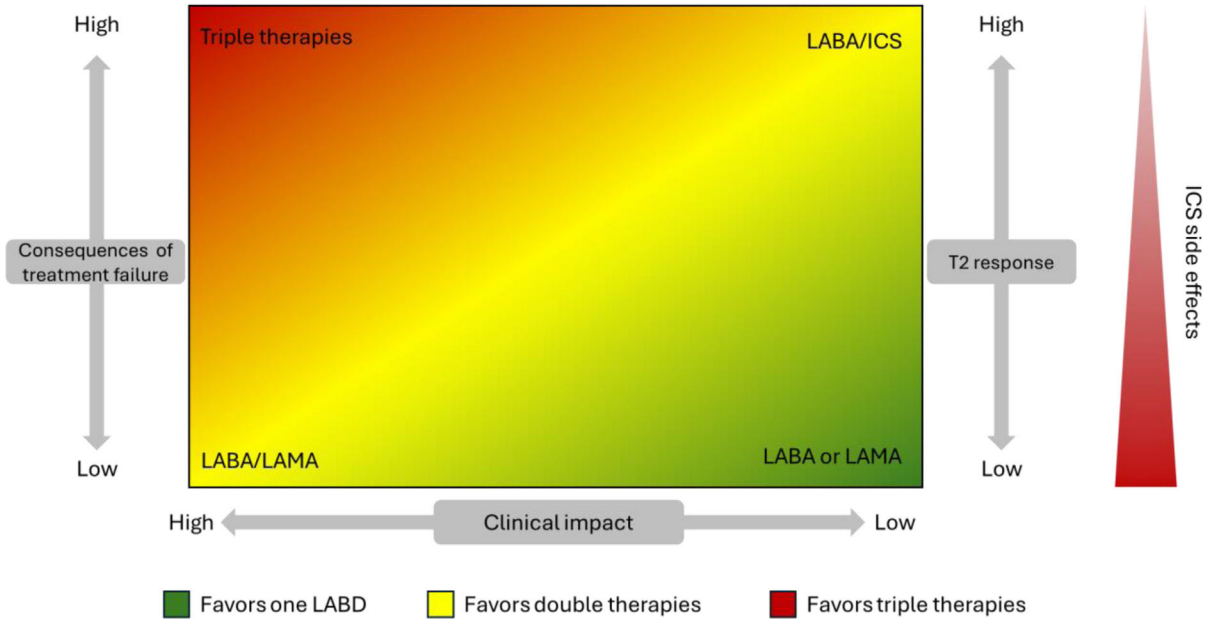


Fig. 1. The COPD kaleidoscope. LABD: long-acting bronchodilators; LABA: long-acting β2 agonist; LAMA: long-acting muscarinic antagonist; ICS: inhaled corticosteroids.

https://doi.org/10.1016/j.arbres.2024.11.010

Please cite this article as: J.M. Figueira-Gonçalves and J.L. Lopez-Campos, The COPD Kaleidoscope: Breaking Bad Dogmatic Recommendations, Archivos de Bronconeumología, https://doi.org/10.1016/j.arbres.2024.11.010

stand out as critical for guiding inhaled therapy in COPD: (1) the clinical impact of the disease on daily activities, (2) the presence of T2 inflammation, (3) the risk of adverse effects, and (4) the potential consequences of treatment failure. These variables can be envisioned as elements of a "kaleidoscope" (Fig. 1), wherein each case requires a unique combination of factors to guide clinical decisions. For instance, patients experiencing significant symptomatic burden may benefit from more intensive bronchodilator therapy. Similarly, the risk of therapeutic failure, particularly in individuals with extensive comorbidities or severe disease, warrants careful consideration to prevent adverse outcomes. The presence of T2 inflammation serves as another pivotal determinant, often indicated by peripheral blood eosinophil counts—a surrogate marker recommended by current guidelines. Although the utility and precision of T2 markers remain a topic of ongoing debate,[7,8] advancements in this area may soon provide more reliable indicators. Additionally, a history of adverse reactions to inhaled corticosteroids (ICS) should influence treatment selection, underscoring the importance of balancing efficacy with safety.

The ongoing debate regarding whether COPD treatment should commence with maximal therapy or follow a stepwise escalation highlights the need for flexible, evidence-informed decision-making.[9] Beyond this dichotomy, clinicians must adopt a more adaptable framework, refining treatment plans as clinical determinants unfold over time. In a disease characterized by its progressive nature, selecting appropriate maintenance therapy is critical for achieving sustained control over clinical manifestations. This perspective challenges static, dogmatic treatment paradigms. Instead, COPD management should embrace a dynamic, patient-centered approach, adapting therapeutic strategies to evolving clinical scenarios.

Drawing inspiration from the popular television series *Breaking Bad*, we advocate "breaking bad" from rigid therapeutic recommendations that portray COPD management as static and universally applicable. Effective clinical practice demands a dual focus: integrating insights from clinical trials while acknowledging the multifaceted nature of COPD in real-world settings. By understanding the interplay of pharmacological mechanisms, disease characteristics, and patient-specific factors, clinicians can make informed decisions that pave the way for truly personalized medicine, enabling patients to lead active and fulfilling lives.

Authors' Contributions

All authors have contributed intellectually, comply with the conditions of authorship and have approved the final version.

Declaration of Artificial Intelligence

The submitted manuscript has not been produced in whole or in part with the help of generative artificial intelligence software or tools.

Funding

No funding was provided for the preparation of this manuscript.

Conflict of Interest

JMFG has received fees and financing from (alphabetical order): AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, Faes, Ferrer, Gebro Pharma, GlaxoSmithKline, Laboratories Esteve, Menarini, MundiPharma, Rovi, Novartis.

JLLC has received honoraria during the last 3 years for lecturing, scientific advice, participation in clinical studies or writing for publications for (alphabetical order): AstraZeneca, Bial, Boehringer, Chiesi, CSL Behring, Faes, Gebro, Grifols, GSK, Menarini, Zambon.

References

1. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med. 2001;163:1256–76.
2. Agusti A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, et al. Global initiative for chronic obstructive lung disease 2023 report: GOLD executive summary. Arch Bronconeumol. 2023;59:232–48.
3. Halpin DM, Kerkhof M, Soriano JB, Mikkelsen H, Price DB. Eligibility of real-life patients with COPD for inclusion in trials of inhaled long-acting bronchodilator therapy. Respir Res. 2016;17:120.
4. Pahus L, Burgel PR, Roche N, Paillasseur JL, Chanez P. Initiatives Bsc. Randomized controlled trials of pharmacological treatments to prevent COPD exacerbations: applicability to real-life patients. BMC Pulmon Med. 2019;19:127.
5. Calle Rubio M, López-Campos JL, Miravitlles M, Soler Cataluña JJ, Alcázar Navarrete B, Fuentes Ferrer ME, et al. Variations in chronic obstructive pulmonary disease outpatient care in respiratory clinics: results from the 2021 EPOCONSUL audit. Arch Bronconeumol. 2023;59:295–304.
6. Lopez-Campos JL, Navarrete BA, Soriano JB, Soler-Cataluna JJ, Gonzalez-Moro JMR, Ferrer MEF, et al. Determinants of medical prescriptions for COPD care: an analysis of the EPOCONSUL clinical audit. Int J Chron Obstruct Pulmon Dis. 2018;13:2279–88.
7. Mathioudakis AG, Bate S, Sivapalan P, Jensen JS, Singh D, Vestbo J. Rethinking blood eosinophils for assessing inhaled corticosteroids response in COPD: a post hoc analysis from the FLAME trial. Chest. 2024;166:987–97.
8. Saito Z, Yoshida M, Kojima A, Tamura K, Hasegawa T, Kuwano K. Benefits and risks of inhaled corticosteroid treatment in patients with chronic obstructive pulmonary disease classified by blood eosinophil counts. Lung. 2020;198:925–31.
9. Bozaan D, Taylor B, Taylor SP. Start slow and step up or hit hard, step down? Finding the right initial therapy for chronic obstructive pulmonary disease. Ann Am Thorac Soc. 2024;21:1126–8.

Juan Marco Figueira-Gonçalves [a,*], José Luis Lopez-Campos [b,c]

[a] *Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain*
[b] *Unidad Médico-Quirúrgica de Enfermedades Respiratorias, Instituto de Biomedicina de Sevilla, IBiS/Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Spain*
[c] *Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain*

*Corresponding author.
E-mail address: juanmarcofigueira@gmail.com
(J.M. Figueira-Gonçalves).