Archivos de Bronconeumología xxx (xxxx) xxx–xxx

Sociedad Española de Neumología y Cirugía Torácica SEPAR

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Bronconeumología

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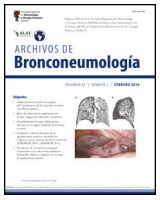

Clinical Letter

Real-world Management of COPD: Dupilumab's Role in Targeting T2 Inflammation as a Treatable Trait

To the Director,

The rise of precision medicine in chronic obstructive pulmonary disease (COPD) has focused attention on identifying phenotypes, endotypes and treatable traits. T2 inflammation, often marked by eosinophilia, is associated with increased exacerbation risk, affecting up to 40% of COPD patients.[1] Dupilumab, a monoclonal antibody targeting the interleukin (IL)-4 receptor alpha subunit, inhibits IL-4 and IL-13 pathways, modulating the T2 inflammatory cascade. Clinical trials like BOREAS and NOTUS have highlighted Dupilumab's efficacy in reducing exacerbations and improving lung function. However, its real-world applicability remains uncertain due to incomplete understanding of T2 inflammation's role in COPD pathogenesis.[2] This study aimed to assess Dupilumab's real-world impact on exacerbation frequency in COPD.

COPD diagnosis followed GOLD guidelines.[3] Patients included had at least 10 pack-year smoking history, persistent non-variable airflow obstruction, negative bronchodilator response, and no asthma history. Patients with at least three severe exacerbations in the prior year enrolled in the "Fragile COPD" program, which emphasized close monitoring, treatment optimization and targeting treatable traits. Exacerbations were classified as moderate (requiring systemic steroids and/or antibiotics) or severe (necessitating hospitalization). Patients with persistent exacerbations despite 12 months of optimized care and peripheral eosinophilia (>300 cells/μL) were eligible for Dupilumab under compassionate use. After the initial supervised dose, all subsequent doses were self-administered. Eosinophilia was monitored quarterly, and lung function reassessed 9–12 months after initiating treatment.

Five patients were included, as detailed in Table 1. All were classified as COPD GOLD 3E and were on triple inhaled therapy (moderate-dose inhaled corticosteroids, long-acting beta-agonists, and long-acting muscarinic antagonists) using a single device. None had a history of childhood asthma; one had atopic dermatitis, while the others lacked type 2 inflammation comorbidities. Peripheral blood eosinophilia remained controlled during Dupilumab treatment, except for one patient who had transient elevation to 1900 cells/μL. One corticosteroid-dependent patient, tapered prednisone from 40 mg to 5 mg daily after Dupilumab treatment. No severe adverse effects occurred. Adherence was good, except for one patient who voluntarily discontinued treatment for two months before resuming.

This real-life case series demonstrates that Dupilumab reduced exacerbation frequency and improved lung function in COPD patients with frequent exacerbations despite optimized therapy. Peripheral eosinophilia is the primary marker of T2 inflammation, though systemic steroid dependence and frequent exacerbations despite optimal treatment may also indicate this phenotype.[4] These findings underscore the importance of identifying treatable traits, aligning with GOLD 2025 guidelines.[3] In COPD patients with uncontrolled comorbidities (like atopic dermatitis), appropriate biologics can help maintain stability. Interestingly, the absence of significant Dupilumab-associated eosinophilia (>2000 cells/μL), contrasts with findings in asthma.[5]

Dupilumab appears to be a safe and promising treatment for selected patients with COPD with frequent exacerbations and elevated eosinophil counts despite optimized therapy and well-managed treatable traits. It may effectively reduce exacerbation frequency, improve lung function and symptoms, and present minimal adverse effects. These findings align with prior clinical trials, including real-world evidence from BOREAS and NOTUS, reinforcing its protentional role in managing this challenging patient's population.

CRediT Authorship Contribution Statement

MJG and AHS contributed to data acquisition, writing and manuscript review. MPD and CAC contributed to patient management and data acquisition. RMDC contributed to data interpretation and manuscript review. All authors approved the final version of the article. All authors contributed equally to this manuscript.

Informed Consent

Each patient provided written informed consent for the publication.

Funding

We declare that this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of Interest

The following authors declare having received fees for lectures and congress participation from the listed companies: MJG (Chiesi, GSK and FAES, Sanofi), RMDC (AstraZeneca, GEBRO, GSK, Sanofi), and AHS (AstraZeneca, GSK, Zambon).

https://doi.org/10.1016/j.arbres.2024.12.014

Please cite this article as: M. Jiménez-Gómez, R.M. Díaz-Campos, M. Padilla-Bernáldez et al., Real-world Management of COPD: Dupilumab's Role in Targeting T2 Inflammation as a Treatable Trait, Archivos de Bronconeumología, https://doi.org/10.1016/j.arbres.2024.12.014

Table 1
Clinical and Functional Characteristics of COPD Patients Under Treatment With Dupilumab.

Characteristic	Case 1	Case 2	Case 3	Case 4	Case 5
Age (years)	87	63	60	71	68
Sex	Male	Male	Female	Male	Male
Smoking history (pack-year index)	Former (35)	Active (78)	Former (40)	Former (80)	Active (110)
Body mass index (kg/m^2)	29	33	17	28	29
Bronchiectasis	–	–	+	–	–
Chronic bronchial infection with *Pseudomonas aeruginosa*	+	–	–	–	–
Continuous home oxygen therapy	–	–	+	–	–
Chronic NIV	–	–	+	–	–
Peripheral eosinophil count (cells/μL)	800	1000	300	500	400
Basal FVC (mL, % predicted)	1890 (65)	3160 (74)	1770 (55)	2620 (68)	3230 (67)
Basal FEV_1 (mL, % predicted)	810 (38)	1190 (36)	970 (39)	1120 (38)	1560 (42)
Basal FEV_1/FVC (%)	43	38	55	43	48
Basal DLCO (% predicted)	72	74	31	46	64
Systemic corticosteroid dependent	–	–	+	–	–
Additional drug controller	Roflumilast	–	Azithromycin –theophylline	Theophylline	Azithromycin
Reason of indication of Dupilumab	Frequent exacerbations				Atopic dermatitis
Moderate–severe exacerbations (last year), prior/after treatment	8 to 2	7 to 3	7 to 5	6 to 1	0 to 0
Change FEV_1 (mL, % predicted), prior/after treatment	+360 (+17%)	+290 (+8%)	N/A	−50 (−1%)	+100 (+3%)
CAT score, prior/after treatment	21 to 12	16 to 15	23 to 24	19 to 15	5 to N/A
mMRC score, prior/after treatment	2 to 1	3 to 1	3 to 3	3 to 2	1 to 1

CAT: COPD assessment test; DLCO: diffusing capacity of the lung for carbon monoxide; FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity; IQR: interquartile range; mMRC: modified Medical Research Council; N/A: not applicable; NIV: non-invasive ventilation. "–": absent. "+": present.

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