Sesión Clínica NEUMOSUR

La EPOC que viene

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Hospital Universitario de Jaén

Conflictos de interés

- Financiación para formación, reuniones, cursos y congresos en los últimos 3 años por:
  - Astra Zeneca
  - Bial
  - Chiessi
  - Faes
  - GSK
  - Teva

- Honorarios como ponente en los últimos 3 años para:
  - Astra Zeneca
  - Gebro - Farma
  - Pari
  - Roche
  - Teva

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Card View | Table View

Showing results for: **COPD Chronic Obstructive Pulmonary Disease**

+ Synonyms of conditions or disease (57)

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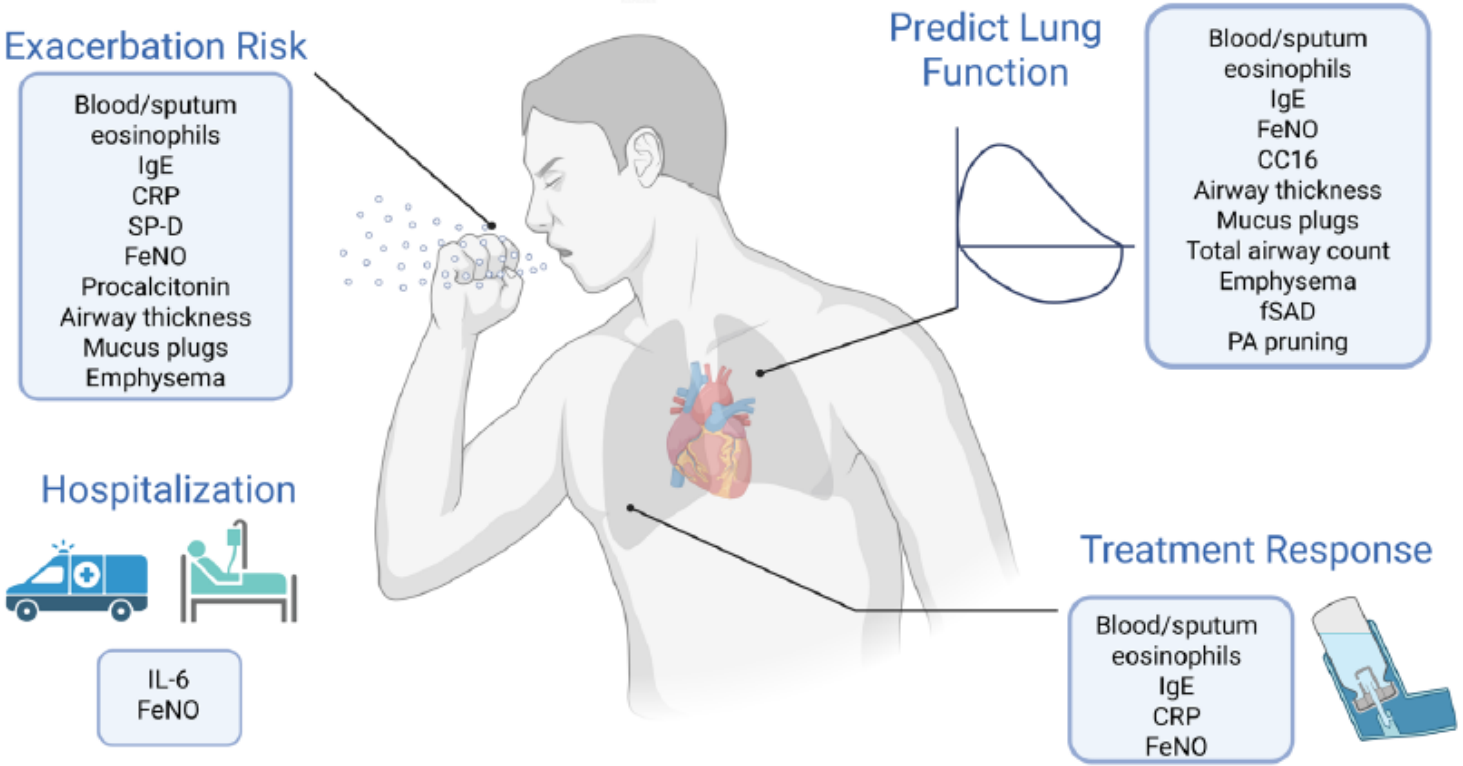
Biomarcadores

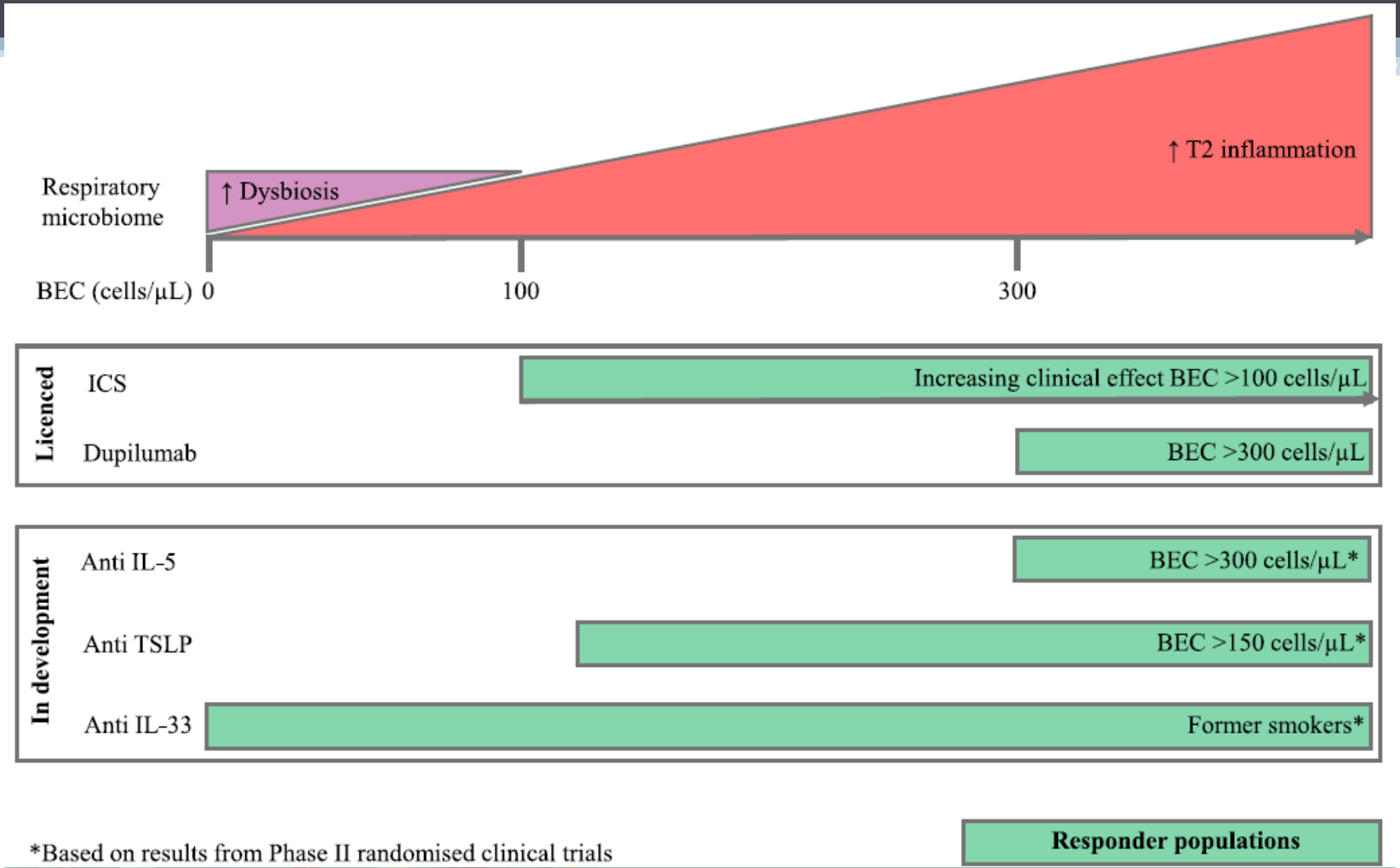
Característica medible que constituye un indicador de un proceso biológico normal o patogénico, de la respuesta a una exposición o intervención

Clinical Applications of Biomarkers in COPD



Abbreviations
CC16 = Club cell secretory protein, CRP = C-reactive protein, FeNO = Fractional exhaled nitric oxide, fSAD = functional small airway disease, IgE= Immunoglobulin E, IL= Interleukin, PA = Pulmonary artery, SP-D = Surfactant protein D

Phillips, K.M.; Lavere, P.F.; Hanania, N.A.; Adrish, M. The Emerging Biomarkers in Chronic Obstructive Pulmonary Disease: A Narrative Review. Diagnostics 2025,15, 1245.



Dave Singh, Andrew Higham, Alexander G. Mathioudakis, Augusta Beech. Chronic Obstructive Pulmonary Disease (COPD): Developments in Pharmacological Treatments. Drugs (2025) 85:911–930

Asociación entre biomarcadores de suero/sangre y aire exhalado con diferentes objetivos en EPOC

Biomarcador	Descenso función pulmonar	Exacerbaciones	Enfisema en imagen	Ingresos	Mortalidad	Predicción de respuesta a tratamientos
Eo sérico	↑	↑				Dupilumab /ICS
IgE	↑	↑				Dupilumab
PCR	↔	↑		¿¿??	¿¿??	Antibiótico en agudizaciones
Fibrinógeno	¿¿??	¿¿??		↔	↑	
Procalcitonina		↑				¿¿ Antibiótico en agudizaciones ??
IL-6				↑	↔	
IL-8		¿¿??			↑	
CC-16	↓				↔	
sRAGE	↔	↔	↓	↔	↔	
FeNO	↑	↑		↑	↑	Dupilumab / ICS

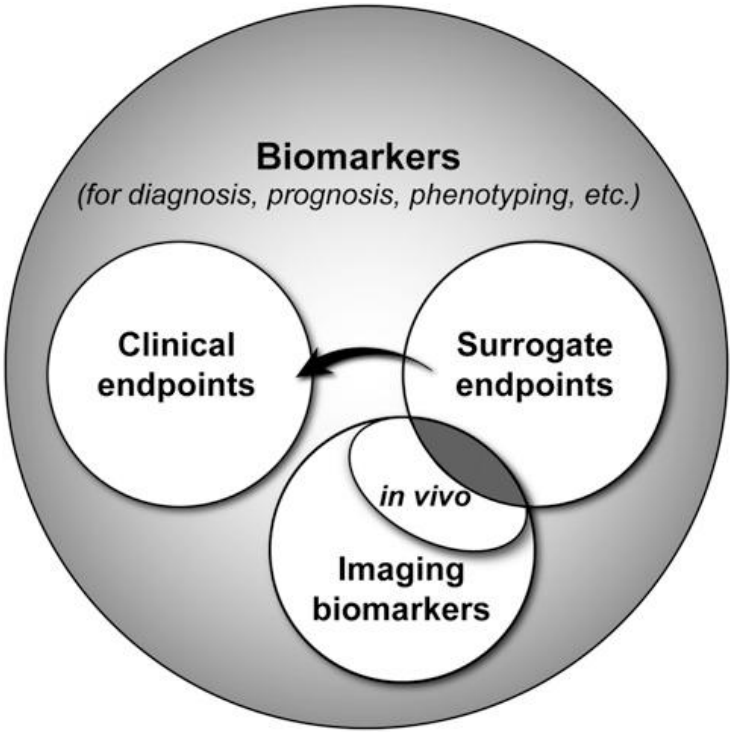
Phillips, K.M.; Lavere, P.F.; Hanania, N.A.; Adrish, M. The Emerging Biomarkers in Chronic Obstructive Pulmonary Disease: A Narrative Review. Diagnostics 2025,15, 1245.

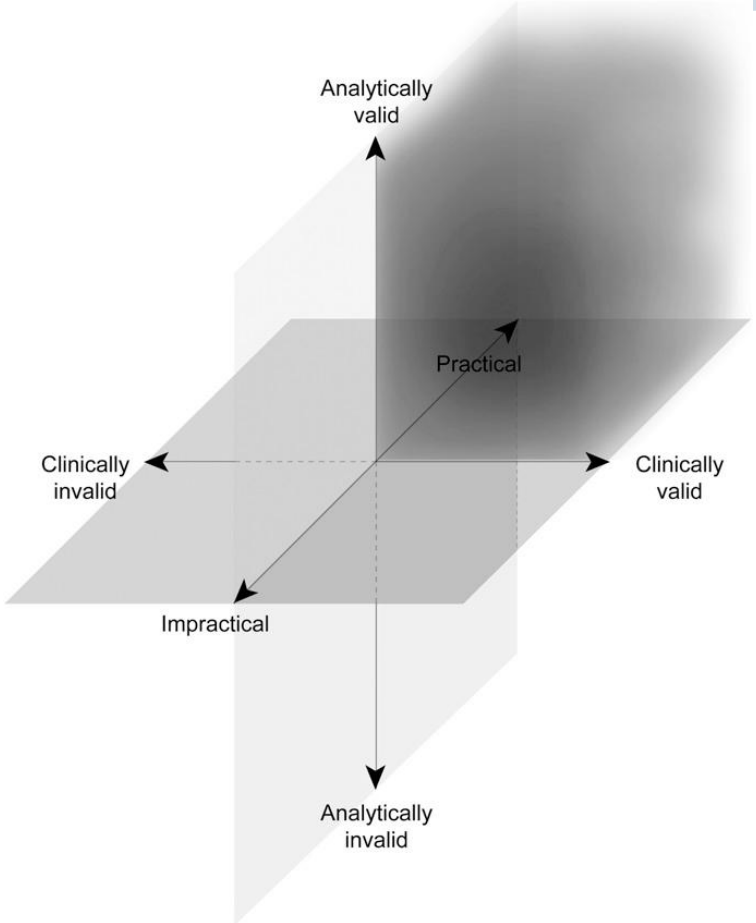
Biomarcadores en esputo

IL-8	Agudizaciones bacterianas
TNF-α	Infecciones bacterianas (Pseudomona aeruginosa) no parece asociarse con agudizaciones, ingresos o mortalidad
Eo >3%	Elevado en biopsias pulmonares en la AEPOC Menor correlación que en el asma entre Eo en esputo y suero
Factor de crecimiento del endotelio vascular (VEGF)	Controvertido

Phillips, K.M.; Lavere, P.F.; Hanania, N.A.; Adrish, M. The Emerging Biomarkers in Chronic Obstructive Pulmonary Disease: A Narrative Review. Diagnostics 2025,15, 1245.

Pruebas de imagen

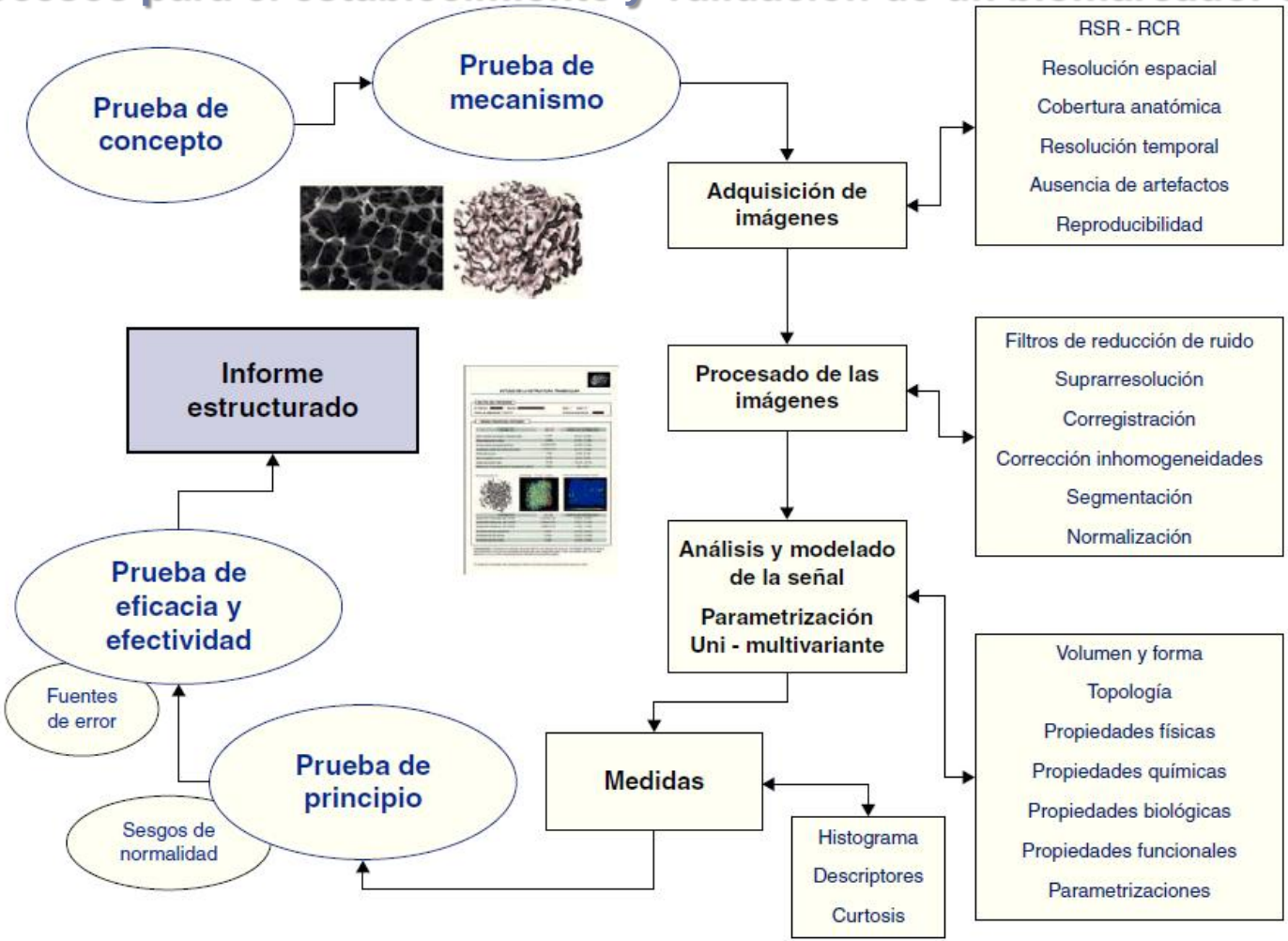




Daniel P. Schuster. The Opportunities and Challenges of Developing Imaging Biomarkers to Study Lung Function and Disease. Am J Respir Crit Care Med Vol 176. pp 224–230, 2007

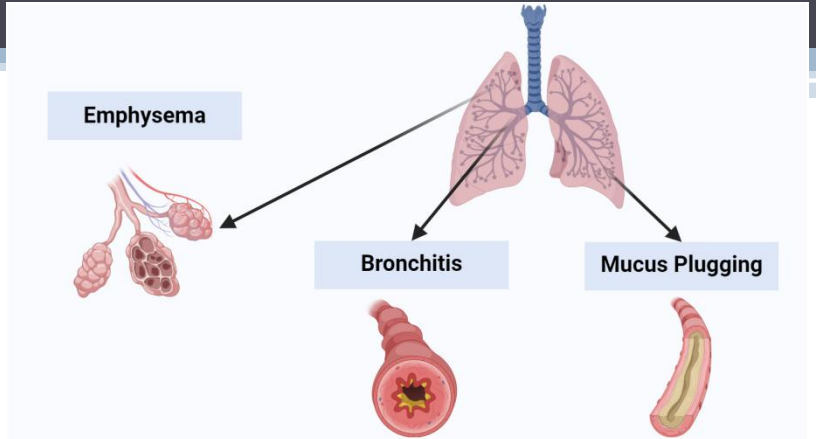
Mapa de procesos para el establecimiento y validación de un biomarcador de imagen

ítems médico-asistenciales



ítems metodológicos

L. Martí Bonmatí et al. Biomarcadores de imagen, imagen cuantitativa y bioingeniería. Radiología. 2012;54(3):269---278



	Emphysema	Bronchitis	Mucus Plugging
CT Biomarker		% Wall Area Total Airway Count	Mucus plug score
Clinical associations		Reduced lung function Symptom progression Loss of independence	Increased mortality Reduced lung function ↑ mMRC
Future imaging biomarker guided treatment?		Anti-inflammatory medications including biologic therapies	Mucolytics and anti-inflammatory medications including biologics

Flynn C, Brightling C.Picture this: The future of imaging biomarkers in COPD. Respirology. 2024;29(11):932–4

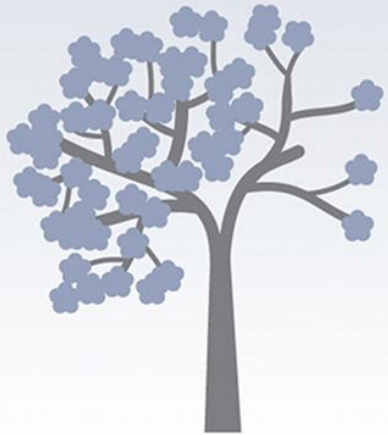
Is Intraparenchymal Vascular Pruning Associated With Progression of Emphysema?

STUDY DESIGN

- **Longitudinal observational study** of current and former smokers with and without COPD
- CT scan at baseline and 5 years
- An automated tool assessed and classified intrapulmonary arteries and veins
- Pulmonary arterial pruning was defined as a lower ratio of small artery volume (<5mm2 cross sectional area) to total lung artery volume

RESULTS

Included 4,227 participants



Greater pruning was associated with

- **More rapid progression of percent emphysema** (0.11 percentage points/year per SD arterial pruning, 95% CI: 0.09, 0.16)
- **Faster decline in FEV1/FVC** (-0.04%/year per SD arterial pruning, 95% CI: -0.008, -0.001)

Pruning was associated with faster progression of emphysema and more rapid decline in lung function in ever-smokers, suggesting pulmonary vascular differences may be relevant in disease progression.

Pistenmaa C, et al. *CHEST* August 2021
@journal_CHEST | https://doi.org/10.1016/j.chest.2021.01.084

CHEST®

Asociación entre biomarcadores de imagen y diferentes objetivos en EPOC

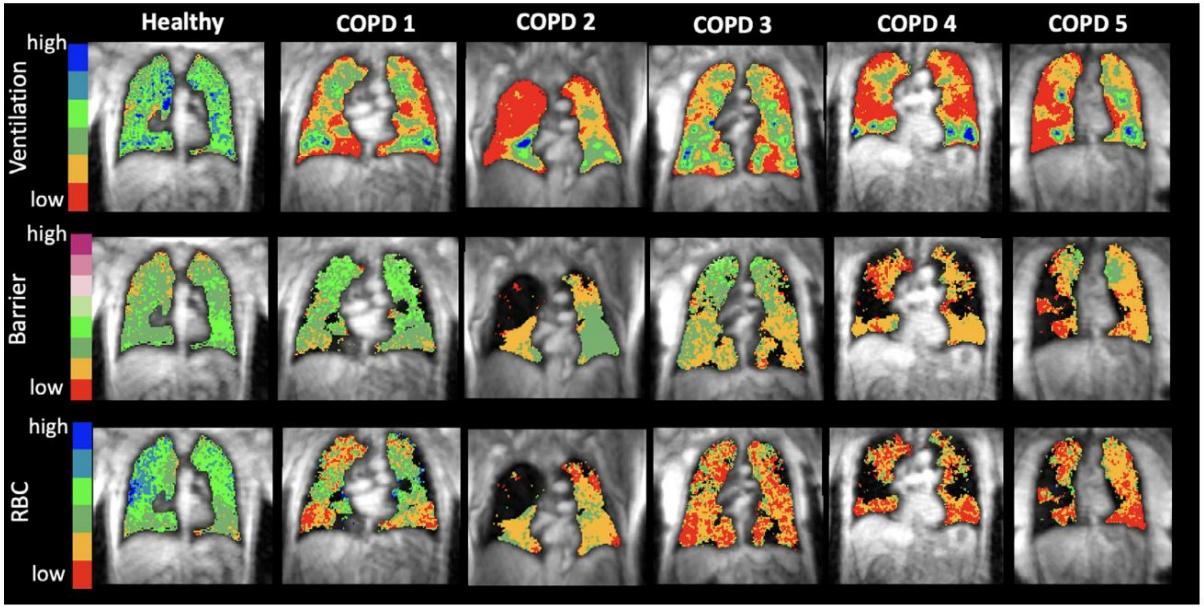
Biomarcador de imagen	↓ de función pulmonar	Riesgo de exacerbación	Dependencia	Mortalidad
Tapones mucosos	↑	↑	↑	↑
Engrosamiento de la pared de las vías respiratorias	↑	↑	↑	↑
Recuento total de vías respiratorias	↑			
* *Enfisema*	↑	↑		↑
* *Afectación funcional de la vía aérea fina*	↑			
Disminución del árbol arterial pulmonar	↑		↑	↑
* *Ensanchamiento de las arterias pulmonares*			↑	↑

Phillips, K.M.; Lavere, P.F.; Hanania, N.A.; Adrish, M. The Emerging Biomarkers in Chronic Obstructive Pulmonary Disease: A Narrative Review. Diagnostics 2025,15, 1245.

Regional Gas Exchange Measured by ^{129}Xe Magnetic Resonance Imaging Before and After Combination Bronchodilators Treatment in Chronic Obstructive Pulmonary Disease

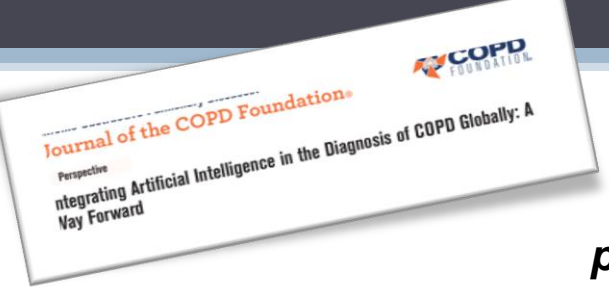
Pruebas de imagen

MRI ^{129}Xe funcional



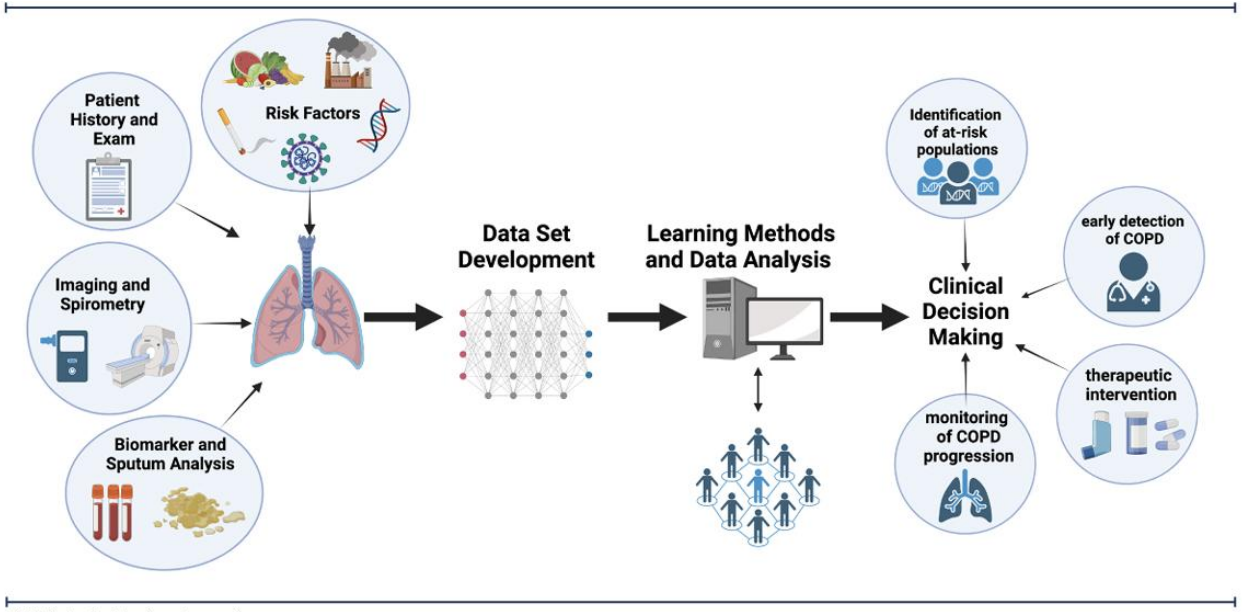
"La resonancia con ^{129}Xe permite cuantificar ventilación y perfusión de forma regional y detectar enfermedad de vía aérea pequeña antes de cambios espirométricos."

J. MAGN. RESON. IMAGING 2021;54:964–974



Pruebas de imagen

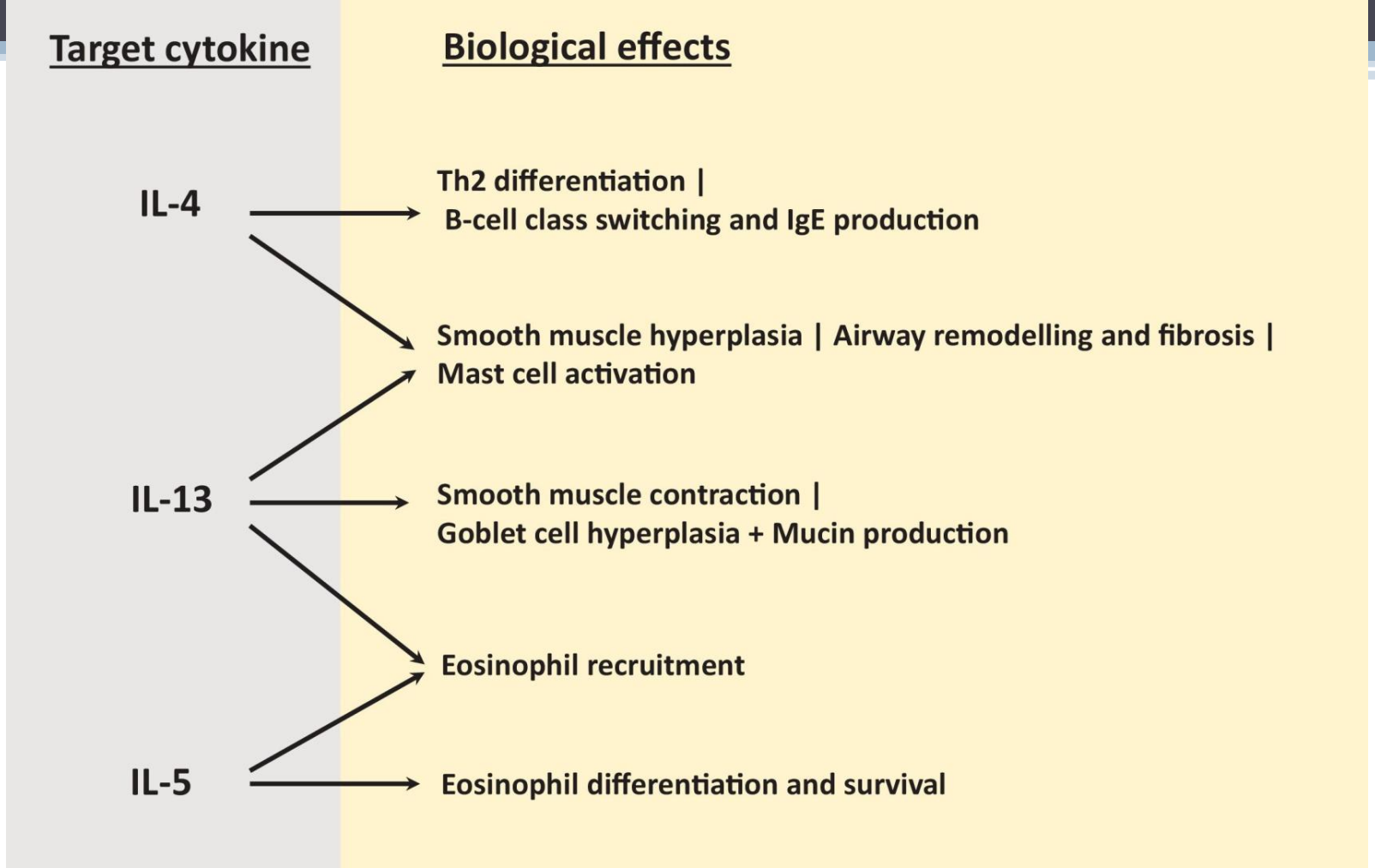
"De la imagen al algoritmo: la IA como herramienta para predecir exacerbaciones y guiar terapias personalizadas"



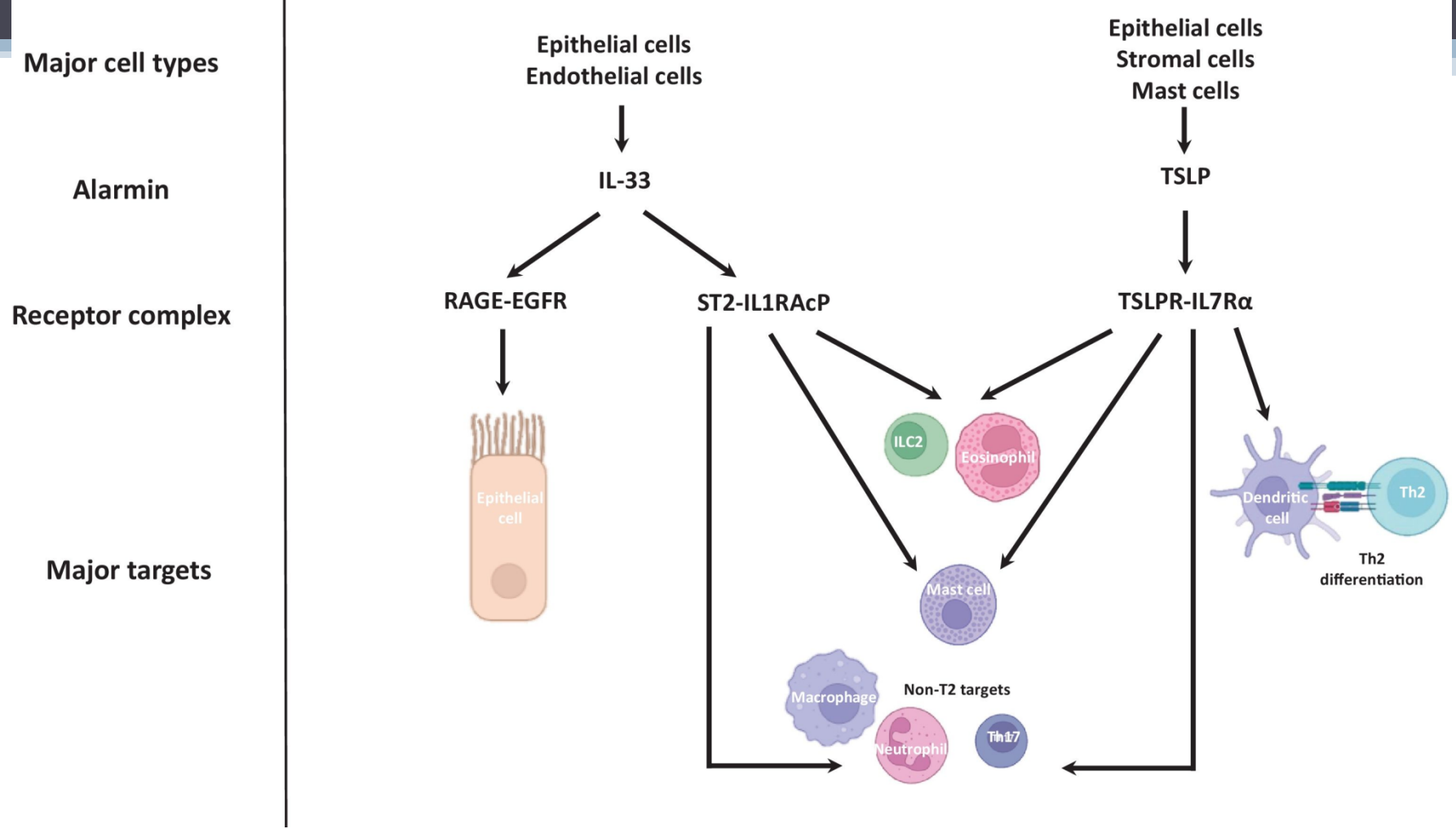
Un enfoque para aplicar e integrar la inteligencia artificial en la práctica clínica

Robertson NM, Centner CS, Siddharthan T. Integrating artificial intelligence in the diagnosis of COPD globally: a way forward. Chronic Obstr Pulm Dis. 2024;11(1):114-120.

Biológicos en la EPOC



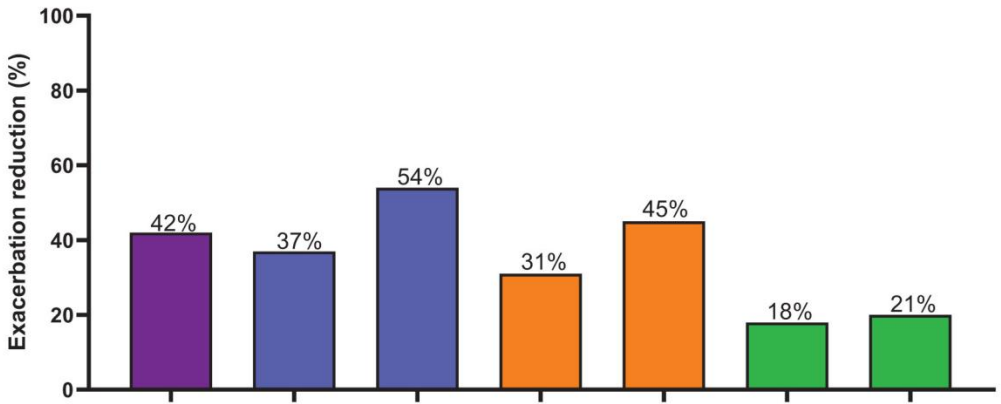
Dave Singh, Antonio Menéndez Lobo, Andrew Higham, Bernardino Alcázar Navarrete Biological Therapy in COPD Management: Current Evidence, Challenges and Opportunities. Available online 20 August 2025, https://www.archbronconeumol.org/es-biological-therapy-in-copd-management-avance-S0300289625002698



Dave Singh, Antonio Menéndez Lobo, Andrew Higham, Bernardino Alcázar Navarrete Biological Therapy in COPD Management: Current Evidence, Challenges and Opportunities. Available online 20 August 2025, https://www.archbronconeumol.org/es-biological-therapy-in-copd-management-avance-S0300289625002698

Responder populations for biological therapies

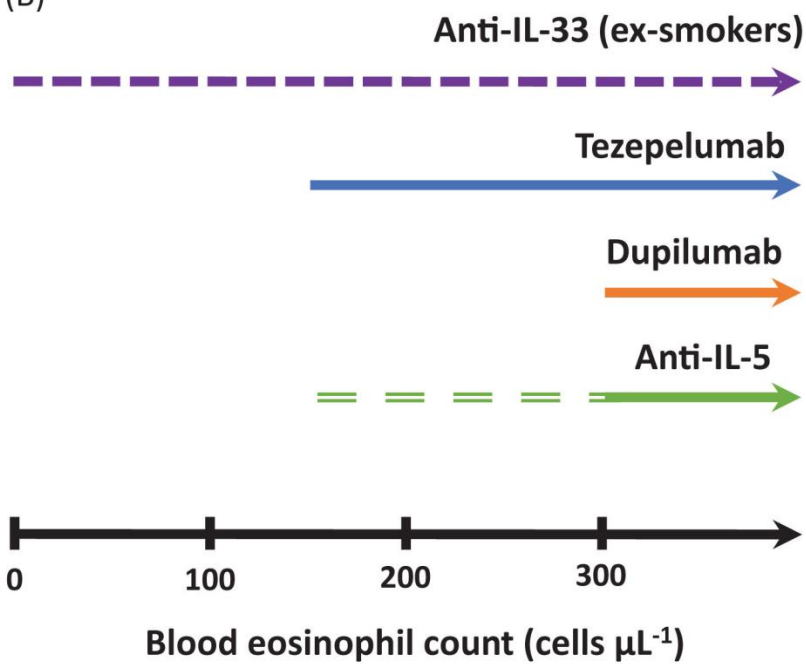
(A)



Drug name	Itepekimab	Tezepelumab	Tezepelumab	Dupilumab	Dupilumab	Mepolizumab	Mepolizumab
Study name	n/a	COURSE	COURSE	Pooled*	Pooled*	METREX	MATINEE
Study design	Phase 2	Phase 2	Phase 2	Phase 3	Phase 3	Phase 3	Phase 3
Population	Ex-smokers	BEC ≥150	FeNO >25	BEC >300	BEC >300+ FeNO >20	BEC>300[a]	BEC>300[b]

*Pooled data from BOREAS and NOTUS studies
[a]BEC ≥150 at screening or >300 historically
[b]BEC ≥150 historically and >300 at screening

(B)



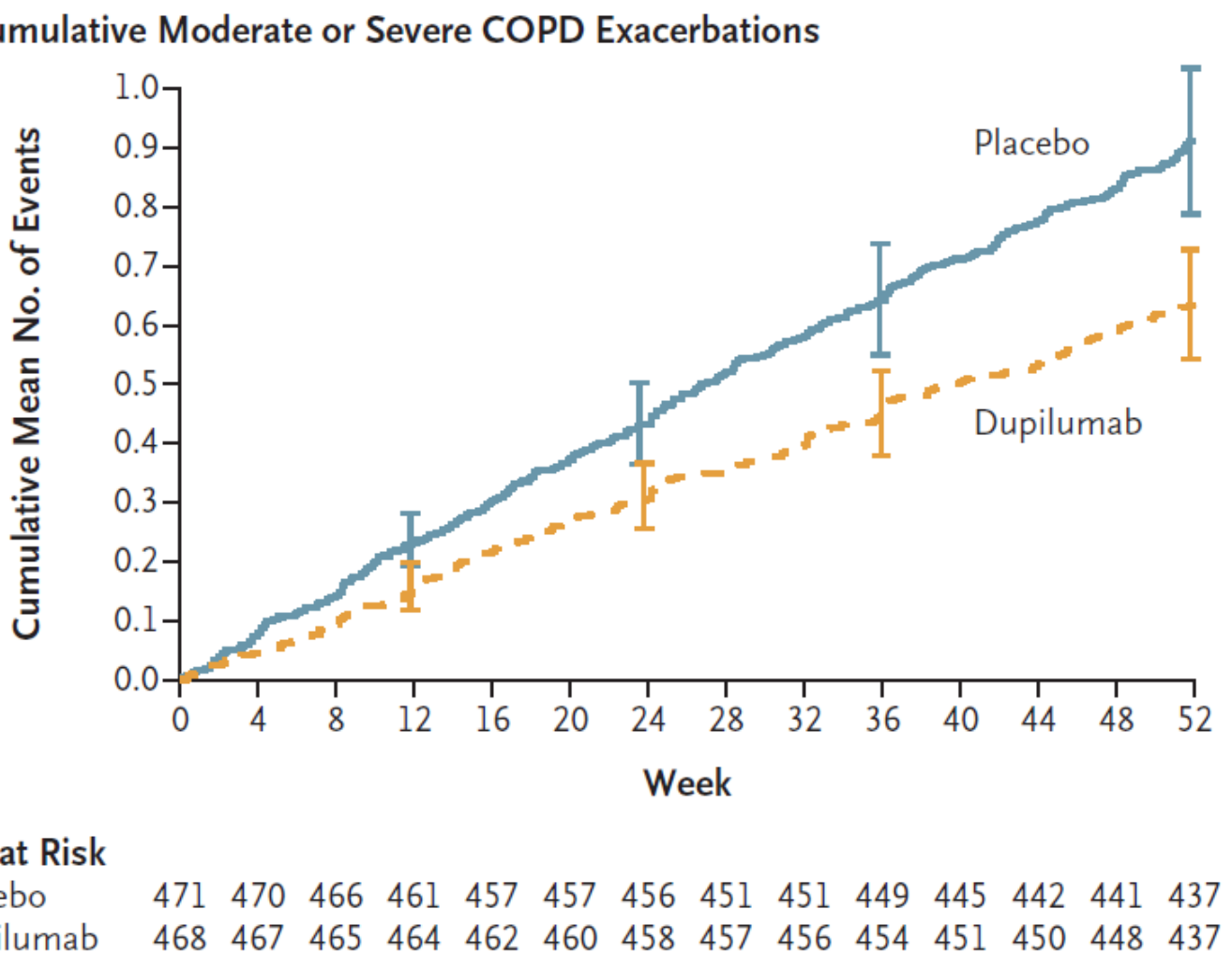
Dave Singh, Antonio Menéndez Lobo, Andrew Higham, Bernardino Alcázar Navarrete Biological Therapy in COPD Management: Current Evidence, Challenges and Opportunities. Available online 20 August 2025, https://www.archbronconeumol.org/es-biological-therapy-in-copd-management-avance-S0300289625002698

Dupilumab en EPOC - BOREAS

Ensayo clínico fase 3, doble ciego	
Población	EPOC con al menos 300 Eo/mcL y con alto riesgo de exacerbaciones, a pesar de estar con triple terapia
Intervención	dupilumab (300 mg) cada dos semanas
Comparador	placebo cada dos semanas
Objetivos	Primario: agudizaciones moderadas o severas Cambio en FEV1 St. George y Evaluating Respiratory Symptoms in COPD

Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts. S.P. Bhatt, K.F. Rabe, et al. N Engl J Med 2023;389:205-14. DOI: 10.1056/NEJMoa2303951

RR 0,70.
IC 95% (0,58-0,86)
p< 0,001



Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts. S.P. Bhatt, K.F. Rabe, et al. N Engl J Med 2023;389:205-14. DOI: 10.1056/NEJMoa2303951

Diferencia de medias de mínimos cuadrados Vs. placebo – 52 semanas: 83 mL.
IC 95% (38-128)
p< 0,001

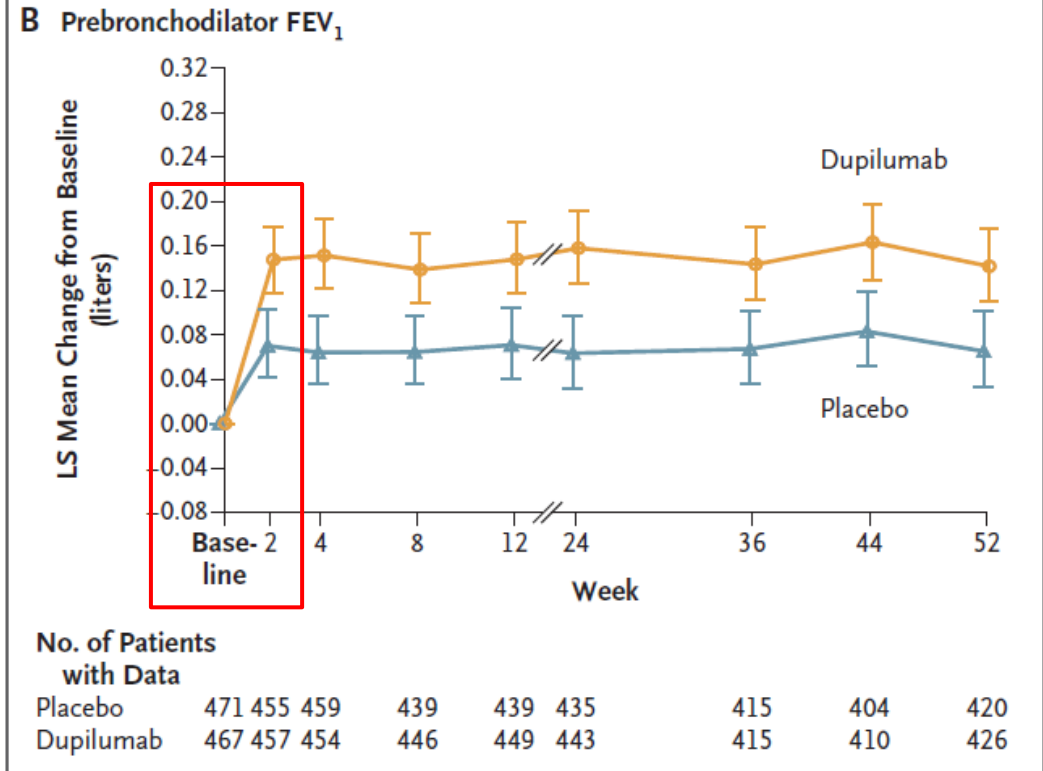


Figure 1. Moderate or Severe COPD Exacerbations and Change in Prebronchodilator FEV_1 over Time.

I bars indicate 95% confidence intervals. COPD denotes chronic obstructive pulmonary disease, FEV_1 forced expiratory volume in 1 second, and LS least squares.

Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts. S.P. Bhatt, K.F. Rabe, et al. N Engl J Med 2023;389:205-14. DOI: 10.1056/NEJMoa2303951

The NEW ENGLAND JOURNAL of MEDICINE

Dupilumab for COPD with Type 2 Inflammation

A PLAIN LANGUAGE SUMMARY

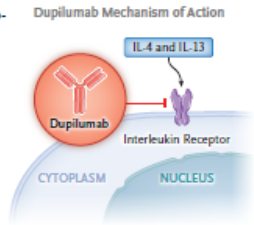
Based on the NEJM publication: Dupilumab for COPD with Blood Eosinophil Evidence of Type 2 Inflammation by S.P. Bhatt et al. (published May 20, 2024)

In this trial, researchers assessed the efficacy and safety of dupilumab in patients with chronic obstructive pulmonary disease (COPD) and evidence of type 2 inflammation, as shown by elevated eosinophil count, plus high exacerbation risk.

Some patients with COPD have evidence of local and systemic type 2 inflammation, including elevated blood eosinophil count. Type 2 inflammation is driven in part by interleukin-4 and interleukin-13.

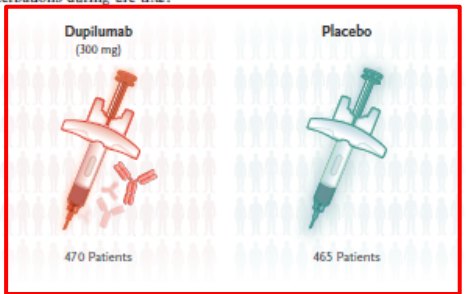
WHY WAS THE TRIAL DONE?

Dupilumab is a fully human monoclonal antibody that blocks the interleukin-4 and interleukin-13 pathways. It is approved for several diseases marked by type 2 inflammation. Whether dupilumab is effective in patients with COPD and eosinophilic evidence of type 2 inflammation is unclear.



HOW WAS THE TRIAL CONDUCTED?

935 patients 40 to 85 years of age who had had COPD exacerbations in the previous year, were taking triple inhaler therapy, and had a blood eosinophil count of at least 300 cells per microliter were assigned to receive add-on subcutaneous dupilumab (300 mg) or placebo every 2 weeks for 52 weeks. The primary end point was the annualized rate of moderate or severe COPD exacerbations during the trial.



PATIENTS

WHO

935 adults

40–85 years of age

Men: 68%; Women: 32%

CLINICAL STATUS

Physician-diagnosed COPD at least 12 months

Triple inhaler therapy at least 3 months

At least 2 moderate or 1 severe exacerbation in previous year

Blood eosinophil count at least 300 cells/microliter

TRIAL DESIGN

- PHASE 3
- RANDOMIZED
- DOUBLE-BLIND
- PLACEBO-CONTROLLED
- LOCATION: 29 COUNTRIES
- DURATION: 52 WEEKS

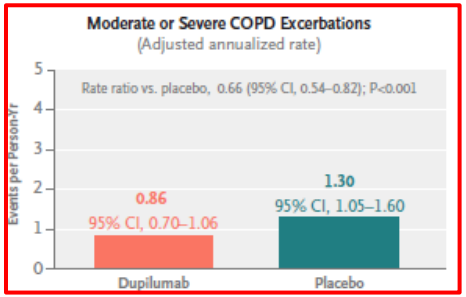
NOTUS

NOTUS

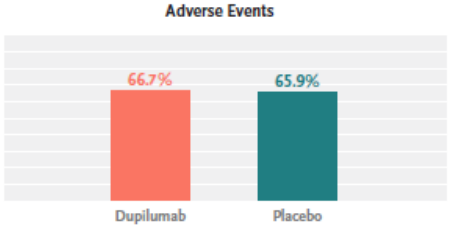
RESULTS

The annualized rate of moderate or severe COPD exacerbations was significantly lower in the dupilumab group than in the placebo group.

The change in prebronchodilator forced expiratory volume in 1 second at weeks 12 and 52 (secondary outcomes) favored dupilumab. Scores on a quality-of-life questionnaire were similar in the two groups.

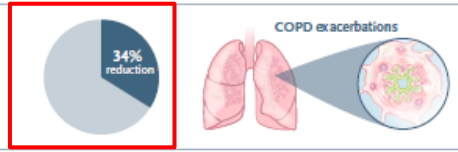


The percentage of patients who had adverse events did not differ between the groups.



EXACERBATIONS

Dupilumab reduced the rate of moderate or severe COPD exacerbations by 34% over 1 year.



LIMITATIONS AND REMAINING QUESTIONS

- 90% of the patients were White.
- The trial was partially conducted during the Covid-19 pandemic. Disruptions in health care and changes in behavior owing to the pandemic led to decreased exposure to viral respiratory infections, which could affect the generalizability of the results.

CONCLUSIONS

In patients with COPD and eosinophilic evidence of type 2 inflammation, the addition of dupilumab to triple inhaled therapy every 2 weeks lowered the incidence of COPD exacerbations over 1 year, as compared with add-on placebo.

LINKS: FULL ARTICLE | NEJM QUICK TAKE

MINISTERIO DE SANIDAD

agencia española de medicamentos y productos sanitarios

INFORME DE POSICIONAMIENTO TERAPÉUTICO

IPT-320/V1/27112024

Informe de Posicionamiento Terapéutico de dupilumab (Dupixent®) en tratamiento de mantenimiento adicional para la enfermedad pulmonar obstructiva crónica (EPOC) no controlada caracterizada por eosinófilos elevados en sangre, en combinación con un corticosteroide inhalado (CEI), un agonista beta-2 adrenérgico de acción prolongada (LABA) y un antagonista muscarínico de acción prolongada (LAMA), o en combinación con un LABA y un LAMA si el CEI no es adecuado

Fecha de publicación: 27 de noviembre de 2024

Indicación autorizada	Situación expediente indicación	Resolución expediente de financiación indicación
Dupixent está indicado en adultos como tratamiento de mantenimiento adicional para la enfermedad pulmonar obstructiva crónica (EPOC) no controlada caracterizada por eosinófilos elevados en sangre, en combinación con un corticosteroide inhalado (CEI), un agonista beta-2 adrenérgico de acción prolongada (LABA) y un antagonista muscarínico de acción prolongada (LAMA), o en combinación con un LABA y un LAMA si el CEI no es adecuado (ver sección 5.1).	En estudio	
Dupixent está indicado para el tratamiento en adultos con prurigo nodular (PN) de moderado a grave que son candidatos para terapia sistémica	Resuelto	Sí, con restricción a la indicación autorizada: -Se limita su uso a pacientes con PN moderado a grave, definido por la presencia de más de 20 lesiones cutáneas, WI-NRS >= 7 (rango de escala: 0

Tezepelumab en EPOC

- Estudio fase IIa → COURSE *
  - Eficacia y seguridad
- Dos ensayos fase III → EMBARK y JOURNEY
  - Eficacia y seguridad
  - Se finalizarán en junio de 2029
- Ensayo fase II UPSTREAM-COPD
  - Efecto en la inflamación de la vía aérea en EPOC de más de 40 años.
  - Cambio Eo, PMN, mastocitos, CD4+, CD8+ y macrófagos
  - Se estima que estará en diciembre de 2025

Efficacy of tezepelumab in patients with moderate to very severe chronic obstructive pulmonary disease with and without chronic bronchitis: phase 2a COURSE study

Diego J Maselli,[1] Mario Castro,[2] MeiLan K Han,[3] Nicole L Martin,[4,5] Nestor A Molfino,[6] Christopher S Ambrose,[7] Navreet S Sindhwani[8] and Sandhia S Ponnarambil[9]

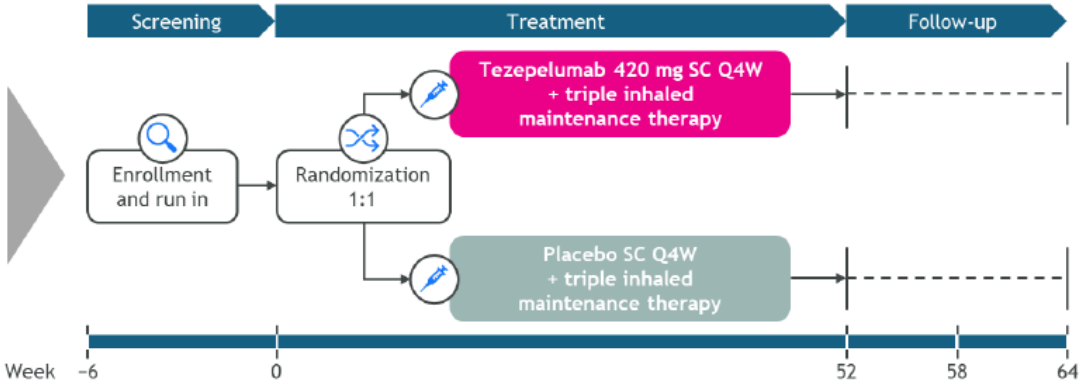
[1]Division of Pulmonary Diseases and Critical Care, Department of Medicine, University of Texas Health San Antonio, San Antonio, TX, USA; [2]Division of Pulmonary, Critical Care and Sleep Medicine, University of Kansas School of Medicine, Kansas City, KS, USA; [3]University of Michigan, Ann Arbor, MI, USA; [4]Biometrics, Late-stage Development, Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Waltham, MA, USA; [5]Cytel Inc., Waltham, MA, USA; [6]Global Development, Inflammation, R&D, Amgen, Thousand Oaks, CA, USA; [7]Respiratory and Immunology, BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, MD, USA; [8]Late-stage Development, Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Durham, NC, USA; [9]Late-stage Development, Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK

American Thoracic Society International Conference, May 16–21, 2025, San Francisco, CA, USA

COURSE (NCT04039113) was a phase 2a, multicenter, randomized, double-blind, placebo-controlled, 52-week study[1]

Inclusion criteria

- Patients 40–80 years old
- Patients with moderate to very severe COPD receiving triple inhaled therapy[a] who experienced ≥ 2 exacerbations in the 12 months before enrollment



Tezepelumab numerically reduced the annualized rate of moderate or severe COPD exacerbations over 52 weeks vs placebo in the overall population by **17% (95% CI: −11, 39; *p* = 0.21)**

Greater reductions in exacerbations were observed in patients with a baseline BEC of ≥ 150 cells/μL (**37% [95% CI: 7, 57]** reduction) and ≥ 300 cells/μL (**46% [95% CI: −15, 75]** reduction)

[a]Patients were considered to be receiving triple inhaled therapy if they had documented use of inhaled corticosteroids, a long-acting β-agonist and a long-acting muscarinic antagonist
BEC, blood eosinophil count; CI, confidence interval; COPD, chronic obstructive pulmonary disease; Q4W, every 4 weeks; SC, subcutaneously

1. Singh D *et al. Lancet Respir Med* 2025;13:47–58

Aims and objectives

¿?

This *post hoc* analysis evaluated tezepelumab efficacy in patients from COURSE with and without SGRQ-defined chronic bronchitis by baseline BEC

A patient was considered to have chronic bronchitis at baseline if their response to **SGRQ items for both cough and phlegm** were "almost every day" or "several days a week" over the past 4 weeks

The following was assessed in patients with and without chronic bronchitis, overall and by baseline BEC (< 150 cells/µL and ≥ 150 cells/µL):

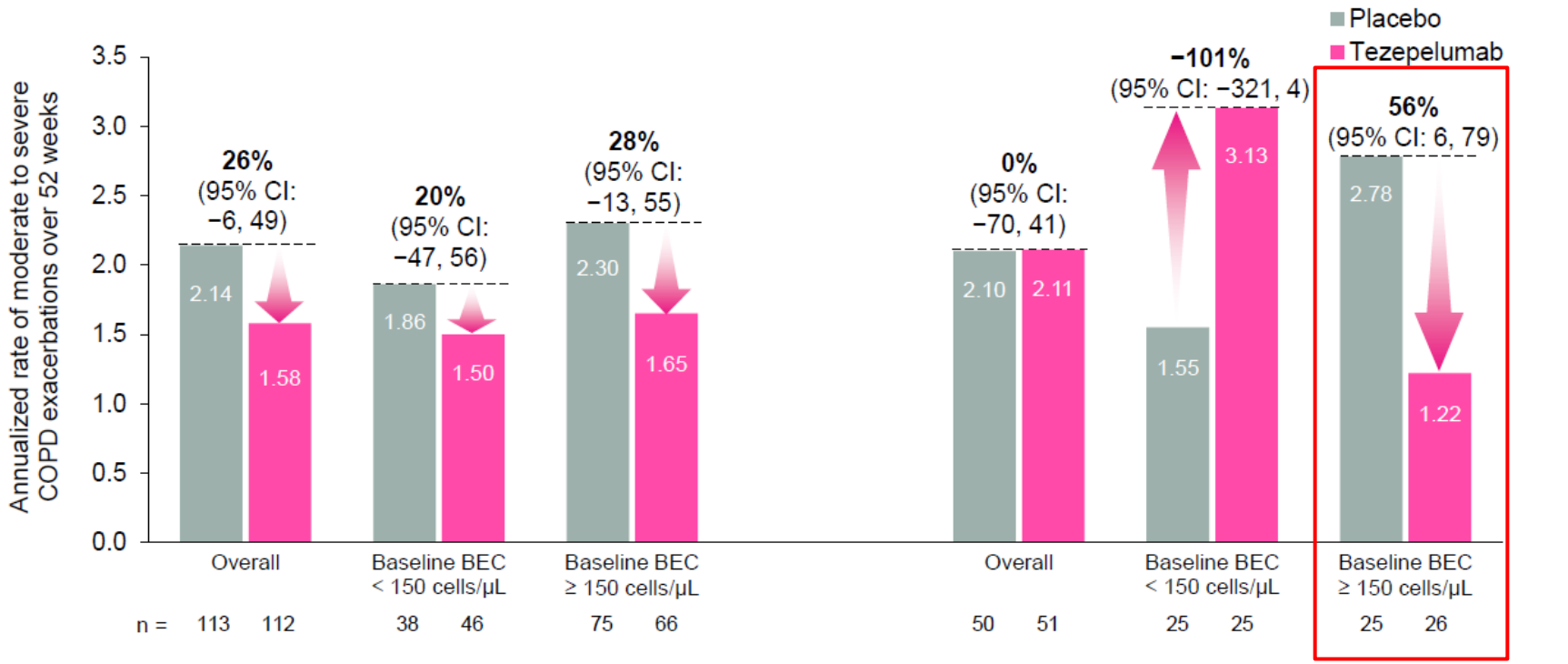
- Annualized rate of moderate or severe COPD exacerbations
- Change from baseline to week 52 in pre-BD FEV_1
- Change from baseline to week 52 in SGRQ total score

The COURSE study did not select for patients with chronic bronchitis. The original definition of chronic bronchitis was determined based on patient responses to questions asked by the investigator and captured in the electronic case report form, without confirmatory diagnosis

BD, bronchodilator; BEC, blood eosinophil count; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; SGRQ, St George's Respiratory Questionnaire

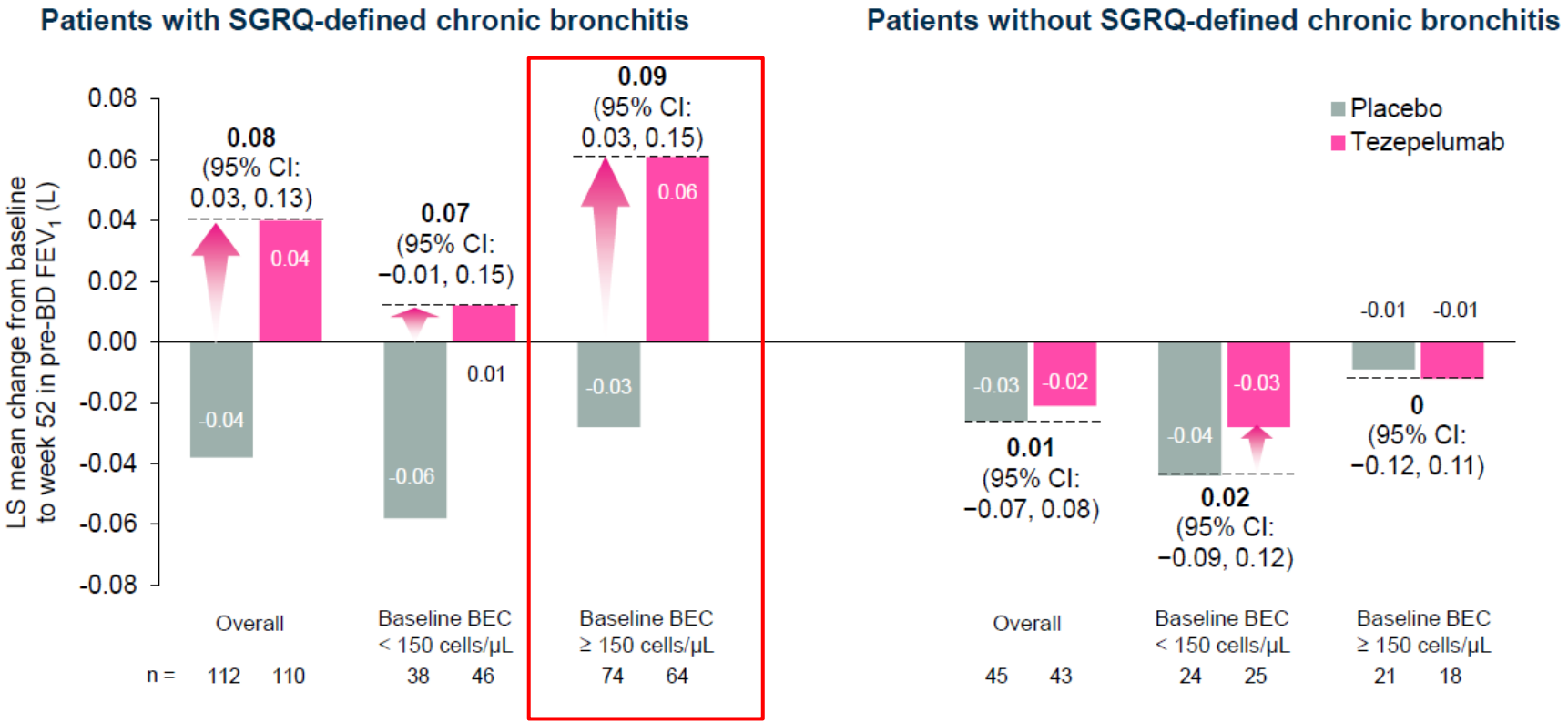
Tezepelumab numerically reduced exacerbations vs placebo among patients with and without chronic bronchitis and a baseline BEC of ≥ 150 cells/µL

¿?



Annualized exacerbation rates were estimated using a negative binomial regression analysis, with treatment, region, number of exacerbations in the year before study entry (2 or ≥ 3), subgroup (if not a covariate) and treatment by subgroup (if not a covariate) as covariates. The values above the bars are percentage reductions with tezepelumab vs placebo
BEC, blood eosinophil count; CI, confidence interval; COPD, chronic obstructive pulmonary disease; SGRQ, St George's Respiratory Questionnaire

Tezepelumab numerically improved lung function vs placebo in patients with chronic bronchitis regardless of baseline BEC



Change from baseline to week 52 in pre-BD FEV_1 was estimated using a repeated measures analysis, with treatment group, region, prior exacerbation count (2, ≥ 3), baseline pre-BD FEV_1, visit, treatment by visit, subgroup (if not a covariate), treatment by subgroup, subgroup by visit and treatment by subgroup by visit as covariates. The values above the bars are LS mean differences between tezepelumab and placebo
BD, bronchodilator; BEC, blood eosinophil count; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; LS, least-squares; SGRQ, St George's Respiratory Questionnaire

Conclusions

In patients with moderate to very severe COPD, tezepelumab recipients with a baseline BEC of ≥ 150 cells/μL with or without chronic bronchitis experienced **numerically fewer COPD exacerbations and greater improvements in health-related quality of life** over 52 weeks versus placebo

Tezepelumab numerically improved lung function in patients with moderate to very severe COPD and **chronic bronchitis** versus placebo

These findings provide **further evidence of and insights into the efficacy of tezepelumab in patients with moderate to very severe COPD**

BEC, blood eosinophil count; COPD, chronic obstructive pulmonary disease

Mepolizumab en EPOC

	METREX	METREO
Población	EPOC con agudizaciones moderadas o severas a pesar de estar con triple terapia inhalada. Subanálisis ≥150 Eo/mcL actual o 300 el año previo	EPOC con agudizaciones moderadas o severas a pesar de estar con triple terapia inhalada. ≥150 Eo/mcL actual o 300 el año previo
Intervención	100 mg de mepolizumab cada 4 semanas	100 o 300 mg de mepolizumab cada 4 semanas
Comparador	Placebo	
Objetivos	Agudizaciones moderadas o severas Seguridad CAT SGRQ	

Mepolizumab por Eosinophilic Chronic Obstructive Pulmonary Disease. I.D. Pavord, et al. N Engl J Med 2017;377:1613-29.DOI: 10.1056/NEJMoa1708208

METREX si Eo +
RR 0,82.
IC 95% (0,68-0,98)
p= 0,04

End Point	METREX Modified Intention-to-Treat Population with an Eosinophilic Phenotype		METREX Overall Modified Intention-to-Treat Population		METREO Modified Intention-to-Treat Population		
	Mepolizumab, 100 mg (N=233)	Placebo (N=229)	Mepolizumab, 100 mg (N=417)	Placebo (N=419)	Mepolizumab, 100 mg (N=223)	Mepolizumab, 300 mg (N=225)	Placebo (N=226)
Primary end point: moderate or severe exacerbations							
Mean annual rate — events/yr†	1.40	1.71	1.49	1.52	1.19	1.27	1.49
Rate ratio vs. placebo (95% CI)	0.82 (0.68 to 0.98)	—	0.98 (0.85 to 1.12)	—	0.80 (0.65 to 0.98)	0.86 (0.70 to 1.05)	—
Adjusted P value	0.04	—	>0.99	—	0.07	0.14	—
Secondary end points							
Time to first moderate or severe exacerbation							
Kaplan–Meier median time to first moderate or severe exacerbation — days	192	141	194	176	267	258	166
Estimated risk of a moderate or severe exacerbation by wk 52 — % (95% CI)‡	64.6 (58.3 to 70.8)	75.2 (69.3 to 80.8)	65.5 (60.7 to 70.1)	71.2 (66.6 to 75.6)	57.9 (51.5 to 64.5)	58.8 (52.4 to 65.3)	66.7 (60.2 to 73.1)
Hazard ratio vs. placebo (95% CI)	0.75 (0.60 to 0.94)	—	0.89 (0.75 to 1.05)	—	0.82 (0.64 to 1.04)	0.77 (0.60 to 0.97)	—
Adjusted P value	0.04	—	>0.99	—	0.14§	0.14§	—
Exacerbations leading to emergency department visit or hospitalization							
Mean annual rate — events/yr†	0.30	0.26	0.29	0.26	0.17	0.23	0.28
Rate ratio vs. placebo (95% CI)	1.16 (0.77 to 1.75)	—	1.10 (0.81 to 1.49)	—	0.59 (0.35 to 0.98)	0.83 (0.51 to 1.34)	—
Adjusted P value	0.60	—	>0.99	—	0.14§	0.45§	—
SGRQ total score at wk 52							
Change from baseline	−2.8±1.1	−3.0±1.1	−3.2±0.8	−4.0±0.8	−5.0±1.0	−3.3±1.0	−3.1±1.0
Difference vs. placebo (95% CI)	0.2 (−2.8 to 3.2)	—	0.7 (−1.5 to 2.9)	—	−1.8 (−4.5 to 0.8)	−0.1 (−2.8 to 2.6)	—
Adjusted P value	>0.99	—	>0.99	—	0.45§	0.93§	—
CAT score at wk 52							
Change from baseline	−0.8±0.5	0.0±0.5	−1.0±0.3	−0.4±0.4	−1.6±0.42	−0.8±0.42	−0.4±0.42
Difference vs. placebo (95% CI)	−0.8 (−2.0 to 0.5)	—	−0.6 (−1.5 to 0.4)	—	−1.1 (−2.3 to 0.0)	−0.4 (−1.5 to 0.8)	—
Adjusted P value	>0.99	—	>0.99	—	0.93§	0.93§	—

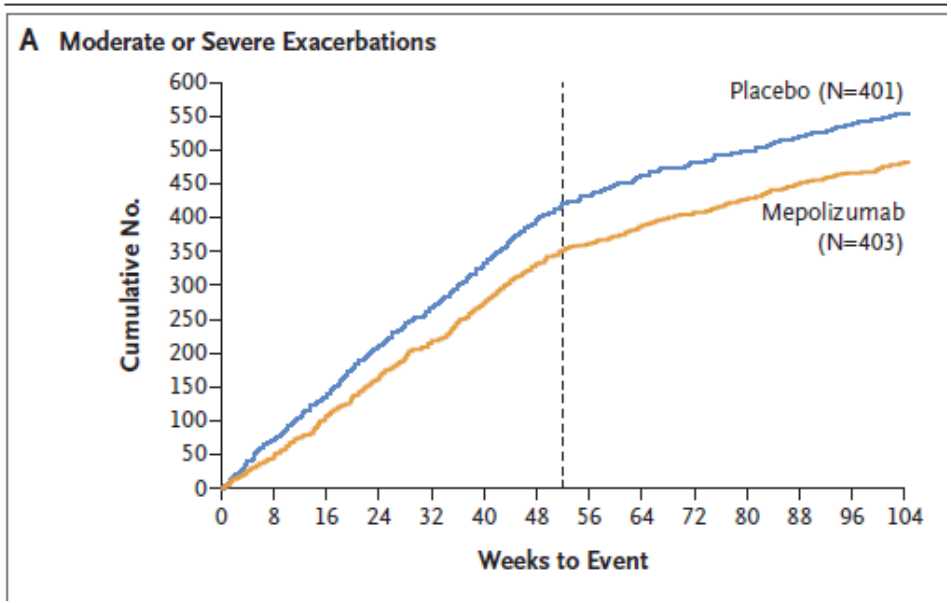
* Plus–minus values are least-squares means ±SE.
† The mean rate is an estimate from the analysis model.
‡ Values were determined with the use of Kaplan–Meier analysis.
§ The results were not significant, in accordance with the prespecified multiple-testing procedure.

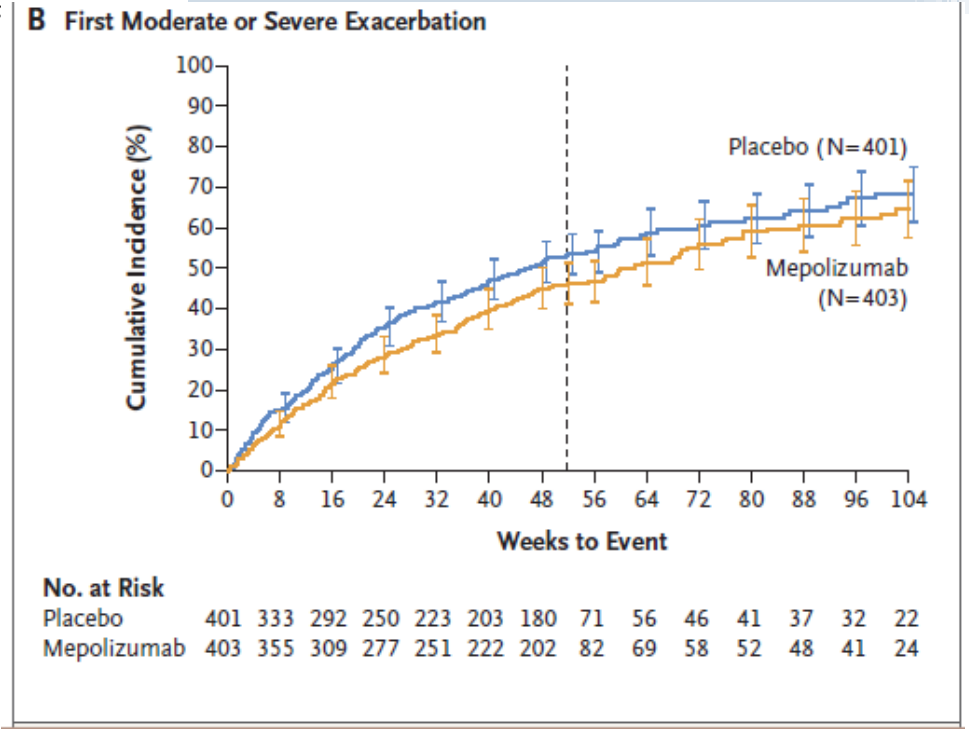
Mepolizumab por Eosinophilic Chronic Obstructive Pulmonary Disease. I.D. Pavord, et al. N Engl J Med 2017;377:1613-29.DOI: 10.1056/NEJMoa1708208

Mepolizumab en EPOC - MATINEE

Ensayo fase 3, doble ciego y controlado con placebo	
Población	EPOC con historia de agudizaciones y al menos 300 Eo/mcL, en tratamiento con triple terapia inhalada
Intervención	Mepolizumab 100 mg cada 4 semanas, durante 52 – 104 semanas
Comparador	Placebo
Objetivos	Primario: ratio anual de agudizaciones moderadas o severas Tiempo hasta la primera agudización moderada o severa Calidad de vida Síntomas Visitas a urgencias o ingresos hospitalarios

Mepolizumab to Prevent Exacerbations of COPD with an Eosinophilic Phenotype. F.C. Sciurba, et al. N Engl J Med 2025;392:1710-20. DOI: 10.1056/NEJMoa2413181





RR Vs placebo 0,79.
IC 95% (0,66-0,94)
p 0,01

HR Vs placebo 0,77.
IC 95% (0,64-0,93)
p 0,009

Mepolizumab to Prevent Exacerbations of COPD with an Eosinophilic Phenotype. F.C. Sciurba, et al. N Engl J Med 2025;392:1710-20. DOI: 10.1056/NEJMoa2413181

Benralizumab en la agudización

Población	Asma o EPOC agudizado, con Eo ≥ 300
1:1:1	*BENRA* + *PRED*: Prenisolona 30 mg/24h/5días + 100 mg Benra SC x 1 *BENRA*: Placebo oral /24h/5días + 100 mg Benra SC x 1 *PRED*: Prenisolona 30 mg/24h/5días + placebo SC x 1

Treating eosinophilic exacerbations of asthma and COPD with benralizumab (ABRA): a double-blind, double-dummy, active placebo-controlled randomised trial, Ramakrishnan, Sanjay et al. Lancet Respir Med 2025; 13: 59–68

	PRED group (n=53)	Pooled-BENRA group (n=105)	p value
Number of patients with treatment failure at 90 days	39 (74%)	47 (45%)	..
Odds ratio (95%CI) *vs* PRED group	..	0·26 (0·13 to 0·56)	0·0005
Change in total VAS symptoms from exacerbation to day 28			
Mean change (95% CI) in mm	103 (75 to 132)	152 (131 to 173)	..
Least-square mean difference *vs* PRED group	..	49 (14 to 84)	0·0065
Change in total VAS cough from exacerbation to day 28			
Mean change (95% CI) in mm	23 (16 to 30)	34 (28 to 39)	..
Least-square mean difference *vs* PRED group	..	10 (2 to 19)	0·020
Change in total VAS dyspnoea from exacerbation to day 28			
Mean change (95% CI) in mm	27 (19 to 34)	34 (28 to 39)	..
Least-square mean difference *vs* PRED group	..	7 (−2 to 16)	0·133
Change in total VAS wheeze from exacerbation to day 28			
Mean change (95% CI) in mm	23 (16 to 29)	36 (32 to 41)	..
Least-square mean difference *vs* PRED group	..	14 (6 to 22)	<0·001
Change in total VAS sputum purulence from exacerbation to day 28			
Mean change (95% CI) in mm	13 (7 to 18)	24 (20 to 28)	..
Least-square mean difference *vs* PRED group	..	11 (4 to 18)	0·002
Change in total VAS sputum volume from exacerbation to day 28			
Mean change (95% CI) in mm	17 (11 to 23)	26 (21 to 30)	..
Least-square mean difference *vs* PRED group	..	9 (2 to 17)	0·016

The VAS was measured on a 100 mm scale for which 0 indicated the best symptoms and 100 indicated the worst symptoms. For VAS the minimal clinical important difference is 9. All analyses were adjusted for randomisation stratification factors namely diagnostic label, steady state FEV$_1$ predicted, number of exacerbations in the previous year, and smoking status. The PRED group indicates the prednisolone only group. The pooled-BENRA group indicates the benralizumab alone and the benralizumab plus prednisolone groups pooled together.

Table 2: **Primary endpoint for the PRED and the pooled-BENRA treatment groups**

OR 0,26.
IC 95% (0,13-0,56)
p= 0,0005

Treating eosinophilic exacerbations of asthma and COPD with benralizumab (ABRA): a double-blind, double-dummy, active placebo-controlled randomised trial, Ramakrishnan, Sanjay et al. Lancet Respir Med 2025; 13: 59–68

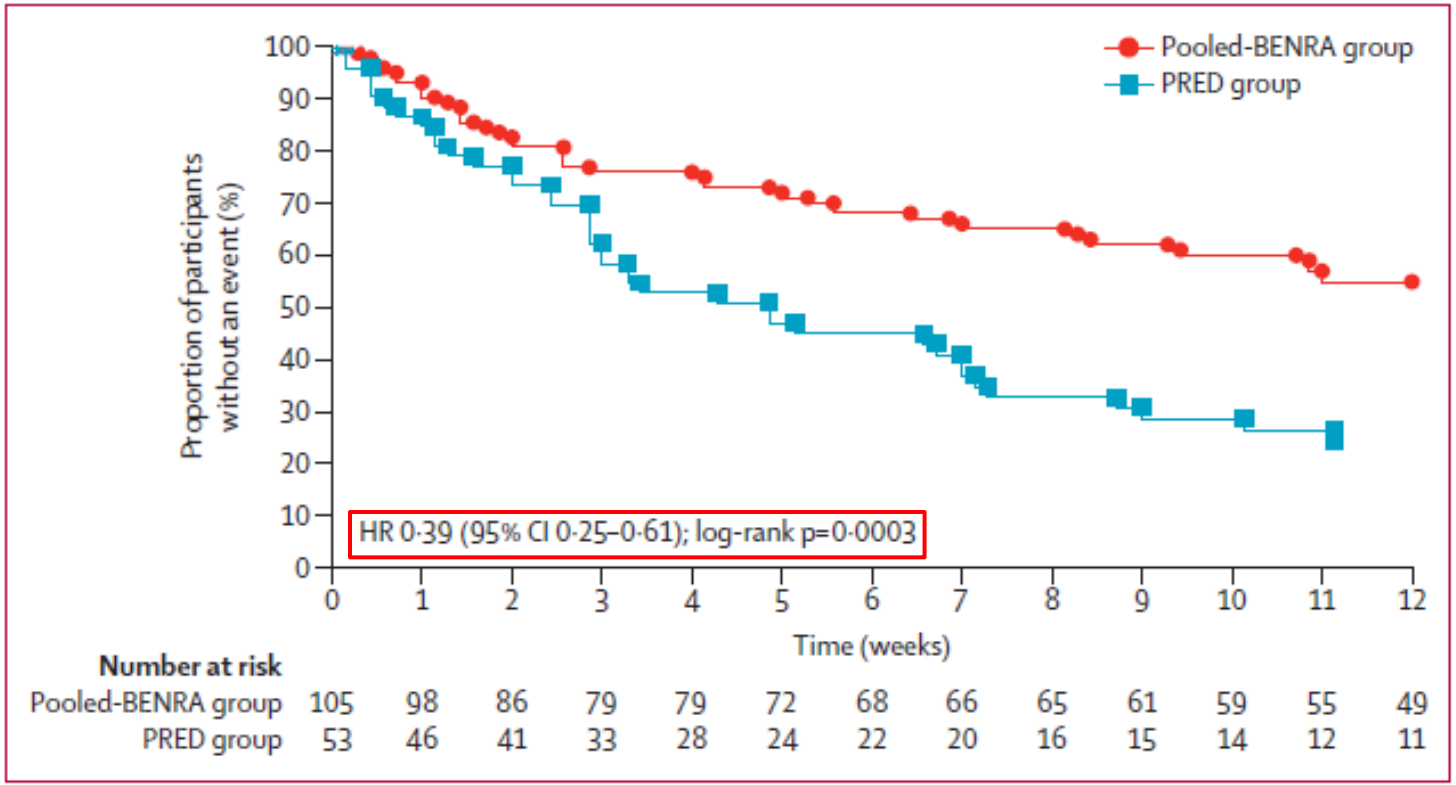


Figure 2: **Kaplan–Meier plot of time to first treatment failure event in the PRED and pooled-BENRA treatment groups**

The PRED group indicates the prednisolone only group (blue line). The pooled-BENRA group indicates the benralizumab alone and the benralizumab plus prednisolone groups pooled together (red line).

Treating eosinophilic exacerbations of asthma and COPD with benralizumab (ABRA): a double-blind, double-dummy, active placebo-controlled randomised trial, Ramakrishnan, Sanjay et al. Lancet Respir Med 2025; 13: 59–68

GALATEA Y TERRANOVA – 2 ensayos complementarios, fase III, de 53 semanas

Población	Pacientes con riesgo de agudización de EPOC moderado o severo, a pesar de estar con ICS/LABA, LABA/LAMA o ICS/LABA/LAMA. Eo>220/mcL	
Intervención	Benralizumab 30 o 100 mg / 4 semanas / 3 dosis → 8 semanas	Benralizumab 10, 30 o 100mg / 4 semanas / 3 dosis → 8 semanas
Comparador	Placebo	
Objetivos	Eficacia en prevenir agudizaciones, en al año de seguimiento Hospitalizaciones Uso de antibióticos o corticoide sistémico Seguridad	
Resultados	**No hay significación estadística en la reducción de agudizaciones** Los efectos adversos son similares al placebo, infecciones respiratorias No hay diferencias en FEV_1 ni calidad de vida **Respondedores a 100mg de Benralizumab: 220 Eo/mcL, con ≥ 3 agudizaciones el año previo y en tratamiento con triple terapia (RR 0,7; IC95% 0,56-0,88)[2]**	

1. Criner GJ, Celli BR, Brightling CE, et al. Benralizumab for the prevention of COPD exacerbations. *N Engl J Med*. 2019;381(11):1023-1034.
2. Criner GJ, Celli BR, Singh D, et al. Predicting response to benralizumab in chronic obstructive pulmonary disease: analyses of GALATHEA and TERRANOVA studies. Lancet. 2020;8:158-170.

Resolute

- Ensayo fase III
- Eficacia y seguridad de Benralizumab 100 mg en pacientes con EPOC exacerbador frecuente y con elevación de Eo sérico[1]
- Nota de prensa: **a pesar de demostrar una mejoría numérica, no se alcanza la significación estadística**[2]
- Datos pendientes de publicar

1, AstraZeneca. Efficacy and safety of benralizumab in moderate to very severe chronic obstructive pulmonary disease (COPD) with a history of frequent exacerbations (RESOLUTE). ClinicalTrials.gov website. https://www.clinicaltrials.gov/ct2/show/NCT04053634
2 AstraZeneca. Update on the RESOLUTE phase III trial for Fasenra in chronic obstructive pulmonary disease [press release]. Published September 17, 2025. https://www.astrazeneca.com/media-centre/press-releases/2025/update-on-resolute-phase-iii-trial.html

Astegolimab (anti ST2) en EPOC

A Phase IIb, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Astegolimab in Patients With Chronic Obstructive Pulmonary Disease	
Población	EPOC, con al menos dos agudizaciones por año, MRCm $\geq$ 2, IPA $\geq$ 10
Intervención	Astegolimab cada 2 o 4 semanas
Comparador	Placebo
Objetivos	Primario: agudizaciones moderadas o severas en el año de seguimiento Calidad de vida Función pulmonar Test de sentarse – levantarse 5 veces

https://clinicaltrials.gov/study/NCT05037929

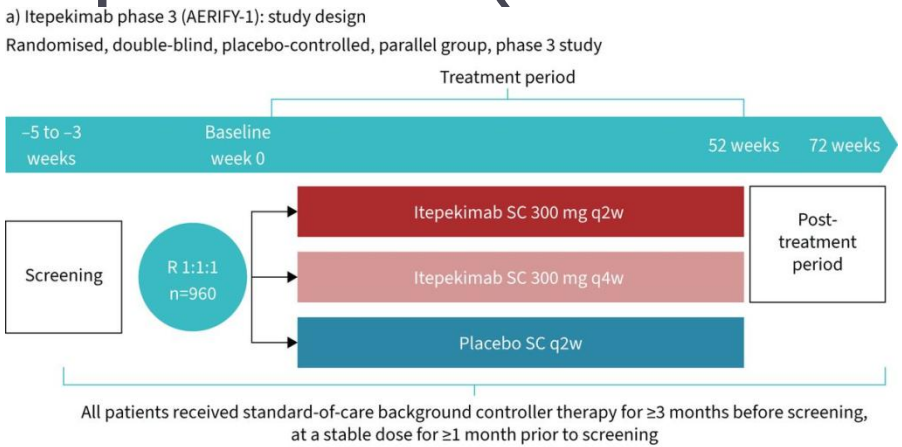
Astegolimab (anti ST2) en EPOC

21/07/2025

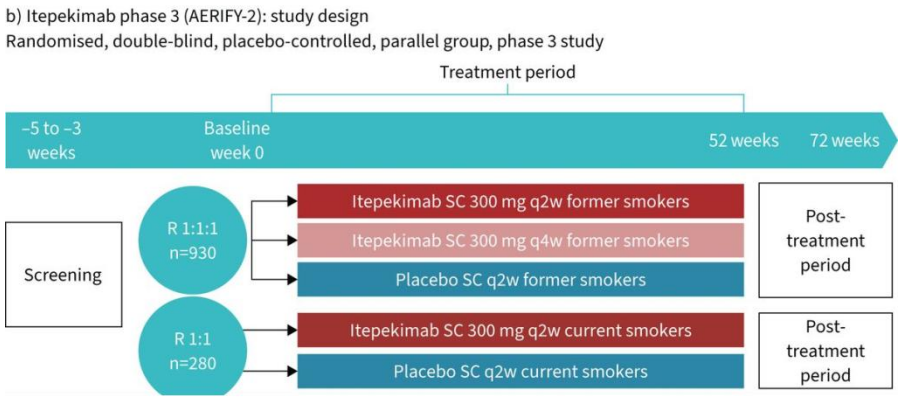
- El estudio pivotal fase IIb **ALIENTO** ha alcanzado el objetivo primario con una **reducción** estadísticamente significativa de la **tasa anualizada de exacerbaciones** (TAE) a las 52 semanas cuando se administró astegolimab cada dos semanas **(15.4%)**
- El estudio **ARNASA** fase III **no alcanzó el objetivo primario** de una reducción estadísticamente significativa de la TAE a las 52 semanas
- El perfil de **seguridad** de astegolimab fue coherente con los datos comunicados anteriormente, sin que se identificaran nuevos signos de seguridad
- El análisis de los datos de los estudios ALIENTO y ARNASA se debatirá con las **autoridades reguladoras** y se presentarán próximamente en un **congreso médico**

https://www.roche.es/actualidad/notas-prensa-producto/2025/julio/roche-proporciona-informacion-actualizada-astegolimab-enfermedad-pulmonar-obstructiva-cronica

Itepekimab (anti-IL-33/IL-1RL1) en EPOC



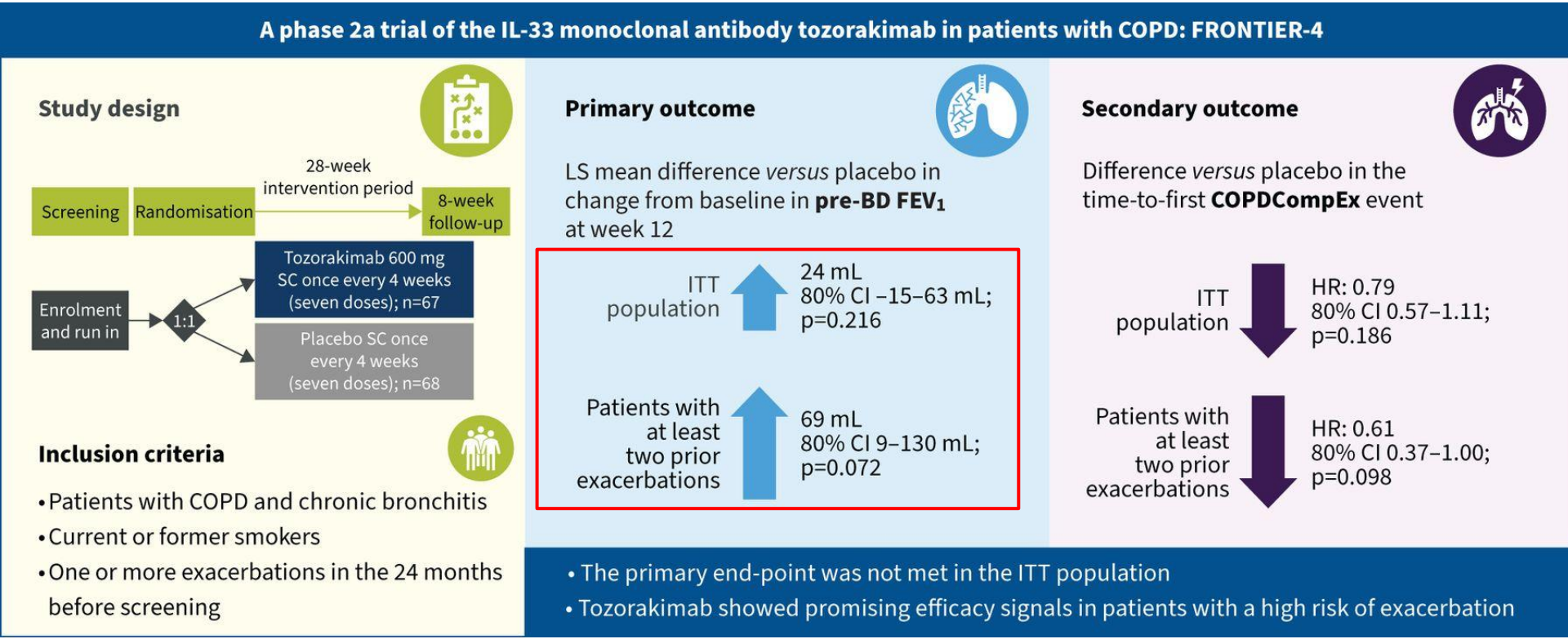
- AERIFY-1 16/12/20 → 28/11/25



- AERIFY-2 12/02/21 → 17/10/25

Rabe KF, Martinez FJ, Bhatt SP, et al. AERIFY-1/-2: 2 phase 3 randomised controlled trials of itepekimab in former smokers with moderate-to-severe COPD. ERJ Open Res 2024; in press

Tozorakimab (anti IL-33) en EPOC



Dave Singh, Patricia Guller et al. A phase 2a trial of the IL-33 monoclonal antibody tozorakimab in patients with COPD: FRONTIER. 66,1, 2402231,2025. Eur Respir J

Tozorakimab (anti IL-33) en EPOC

- Estudio MIRANDA – fase III
  - Agudizaciones en fumadores activos
  - Función pulmonar
  - Calidad de vida
  - Mortalidad

- Estudio PROSPERO – extensión
  - Eficacia y seguridad a largo plazo
  - Reclutamiento activo

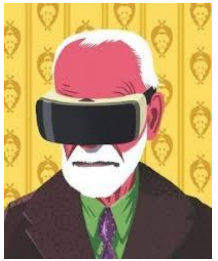
La EPOC que podría venir

WittyDoctor 2.5

PREVENCIÓN

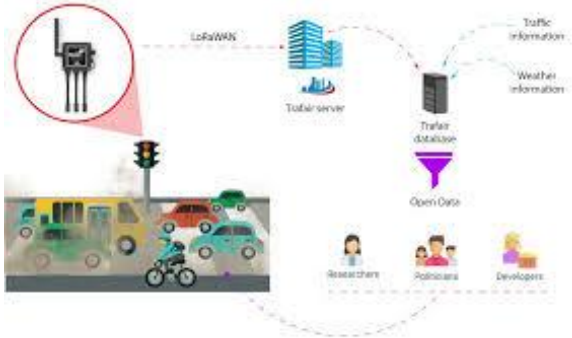
Vacunas preventivas

Cesación tabáquica



Prevención primaria
SERPINA1, CHRNA3/5

Monitorización ambiental



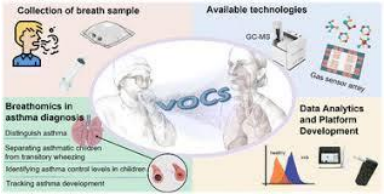
Screening poblacional masivo

WittyDoctor 2.5

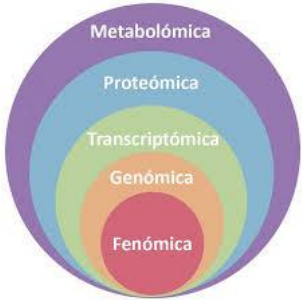
DIAGNÓSTICO

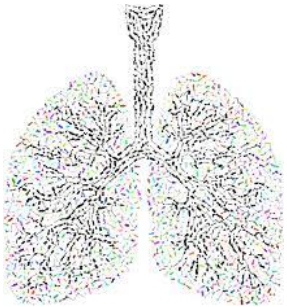
IA en imagen: cuantificar daño, progresión y riesgo

Dxd, inflamación y detectar agudizaciones



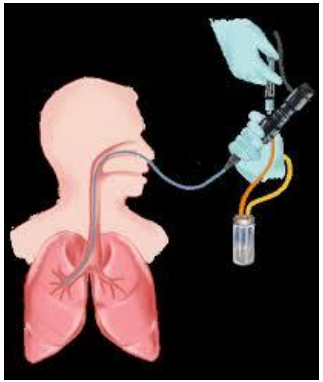
Biomarcadores multiómicos y microbioma





Sensores no invasivos: parámetros respiratorios, Sat O2, FR, tos

Biopsia líquida



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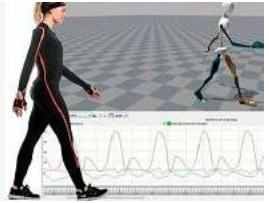
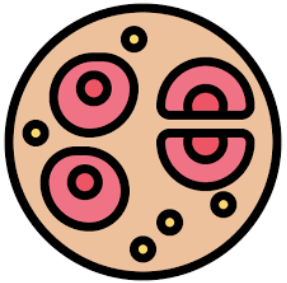
TRATAMIENTO EN FASE ESTABLE

BD ultraprolongados y específicos

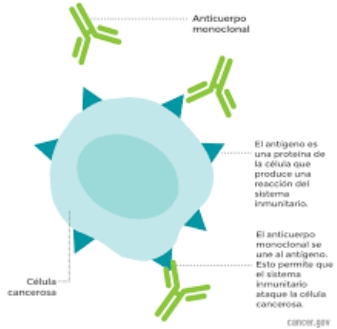
Rehabilitación digital inteligente



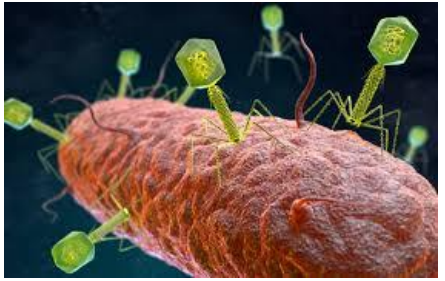
Medicina regenerativa A1AT



AcMo según inflamacion individual



Terapias dirigidas por microbioma



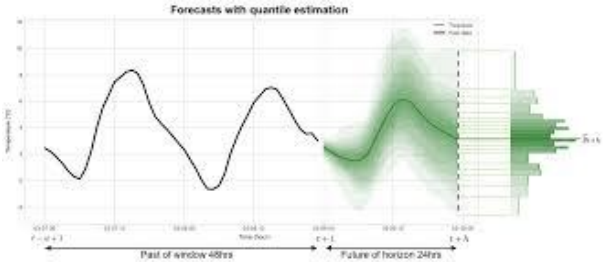
WittyDoctor 2.5

TRATAMIENTO EN AGUDIZACIONES

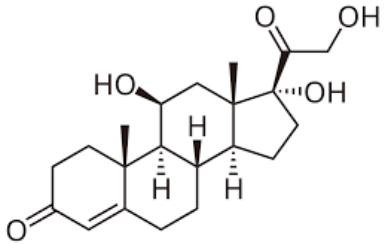
Antibióticos de precisión

Telemonitorización intensiva

Predicción de exacerbaciones

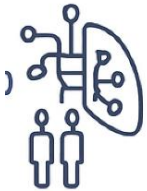


Corticoides inhalados inteligentes



Terapias de rescate avanzadas

Horizonte terapéutico en la EPOC (2025–2030)

Horizonte		Intervención / Mecanismo	Evidencia principal	Estado actual (2025)
2025		**Dupilumab (anti-IL-4/IL-13)** Bloqueo de la inflamación tipo 2 (Th2).	Bhatt SP et al. *N Engl J Med* 2023;389:205-14 (BOREAS). Rabe KF et al. *N Engl J Med* 2024;390:1221-34 (NOTUS). Singh D et al. *Arch Bronconeumol* 2025 (online 20 Ago 2025).	**Realidad clínica** (FDA 2024; EPOC tipo 2 eosinofílica ≥ 300 cél/µL).
2025–2027		**Anti-IL-33 / Anti-ST2 / Anti-TSLP** *(Itepekimab, Tozorakimab, Tezepelumab).*	Rabe KF et al. *ERJ Open Res* 2024 (AERIFY-1/2). Singh D et al. *Eur Respir J* 2025;66:2402231 (FRONTIER). Sverrild A et al. ClinicalTrials.gov NCT05507242 (UPSTREAM-COPD).	**Promesa avanzada** (Fases II–III en curso).
2027–2030		**Combinaciones multi-diana + IA** (bloqueo de alarminas + selección digital por biomarcadores y modelos predictivos).	Phillips KM et al. *Diagnostics* 2025;15:1245 (Biomarcadores emergentes). Flynn C, Brightling C. *Respirology* 2024;29(11):932-4 (Imaging biomarkers). GOLD 2025 Report (Medicina de precisión).	**Futuro cercano** (en validación clínica e implementación digital).

Conclusiones e Hipótesis de Futuro

1.-El futuro de la EPOC posiblemente no va a estar en añadir fármacos, sino en **elegir el tratamiento adecuado para cada paciente, en el momento preciso y con la evidencia correcta**

2.-Pasaremos de tratar la obstrucción a conocer la **biología de la enfermedad** y de medir la función pulmonar a medir el **riesgo individual**

3.-“La EPOC que viene” no será la de nuevos broncodilatadores, sino la de los biomarcadores, la biología inflamatoria y la inteligencia artificial aplicada a la predicción y personalización del tratamiento

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Muchas gracias

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