

# COPD Korea : Year in Review 2025

## COPD의 급성 악화

충남대학교 병원 호흡기알레르기내과  
김소윤



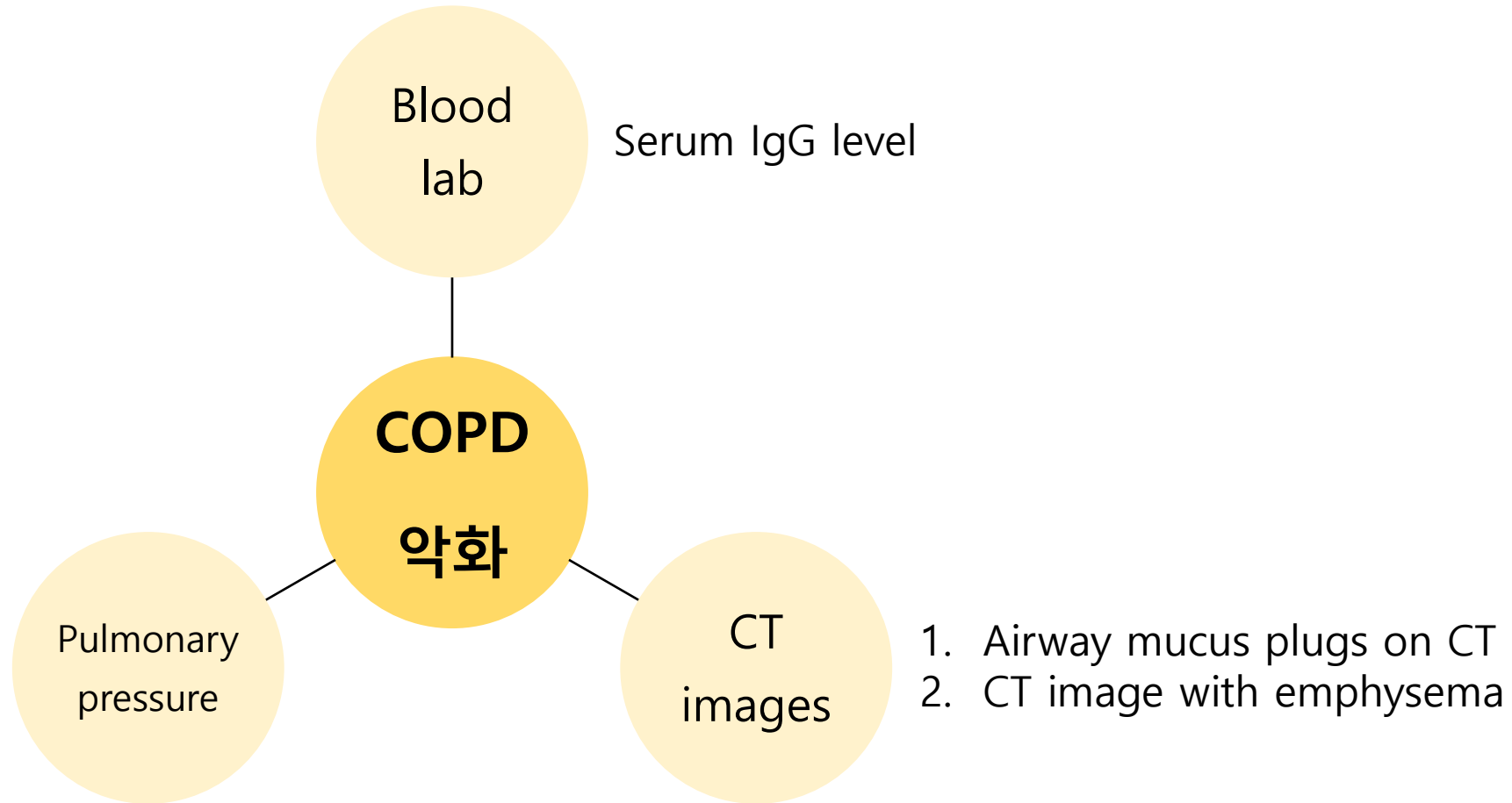


# COPD의 급성 악화

1. COPD Exacerbation의 진단 & 예측인자
2. COPD Exacerbation의 원인
3. COPD Exacerbation의 예방 & 치료



# COPD exacerbation의 진단 & 예측인자





# Blood lab – Serum IgG

ORIGINAL ARTICLE

AJRCCM, 2025/02

## Serum Immunoglobulin G Levels Are Associated with Risk for Exacerbations: An Analysis of SPIROMICS

Michael Burnim<sup>1,2\*‡</sup>, Nirupama Putcha<sup>1\*‡</sup>, David LaFon<sup>3</sup>, Han Woo<sup>1</sup>, Antoine Azar<sup>1</sup>, Lars Groenke<sup>4,5</sup>, Martin Stampfli<sup>4,5</sup>, Alexander Schaub<sup>4,5</sup>, Ashraf Fawzy<sup>1</sup>, Aparna Balasubramanian<sup>1</sup>, Neal Fedarko<sup>1</sup>, Christopher B. Cooper<sup>6</sup>, Russell P. Bowler<sup>7</sup>, Alejandro Comellas<sup>8</sup>, Jerry A. Krishnan<sup>9</sup>, MeiLan K. Han<sup>10</sup>, David Couper<sup>11</sup>, Stephen P. Peters<sup>12</sup>, M. Bradley Drummond<sup>11</sup>, Wanda O'Neal<sup>11</sup>, Robert Paine<sup>13</sup>, Gerard Criner<sup>14</sup>, Fernando J. Martinez<sup>15§</sup>, Jeffrey L. Curtis<sup>10,16</sup>, Graham Barr<sup>17</sup>, Yvonne J. Huang<sup>10</sup>, Prescott Woodruff<sup>18</sup>, Mark Dransfield<sup>9</sup>, and Nadia N. Hansel<sup>1</sup>

### Method – SPIROMICS

- multicenter study of current and former smoker
- 40-80yrs, until July 2015
- First 1497 participants to enroll

1026 with COPD

471 at risk for COPD

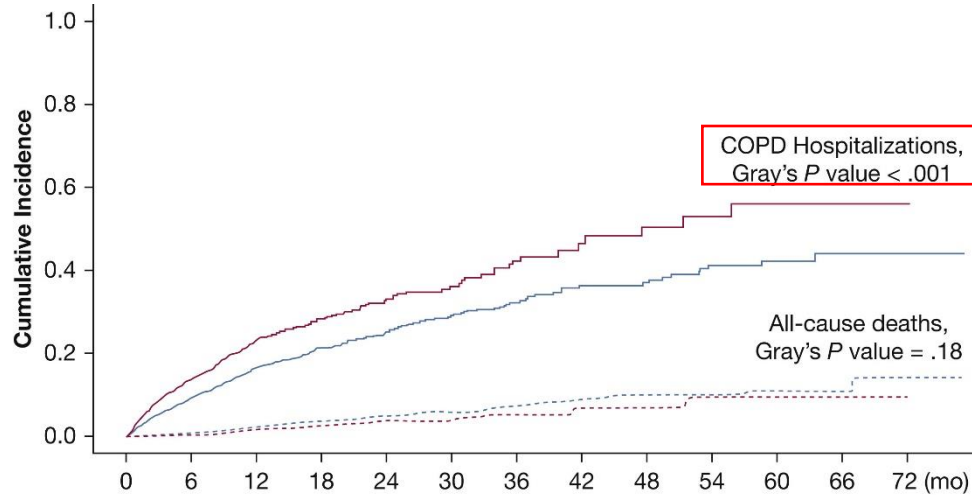
- **Measurement** : ELISA to measure IgG

### Primary outcome

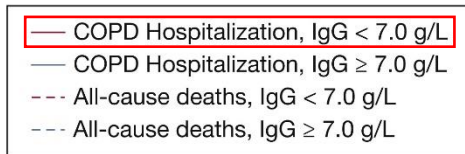
- Risk of any exacerbation and risk of severe exacerbation

### Statistical Methods - Cutoff value of IgG

- 1) 5% increments between the 5th and 50th percentiles of IgG  
→ AIC calculation (lowest AIC = optimal cutoff)
- 2) **35<sup>th</sup> percentile level** or 1,225mg/dL



No. at risk	0	6	12	18	24	30	36	42	48	54	60	66	72 (mo)
IgG < 7.0 g/L	641	531	370	231	183	90	59	27	20	13	6	4	1
IgG ≥ 7.0 g/L	1,618	1,380	961	507	404	255	190	95	80	60	43	15	3

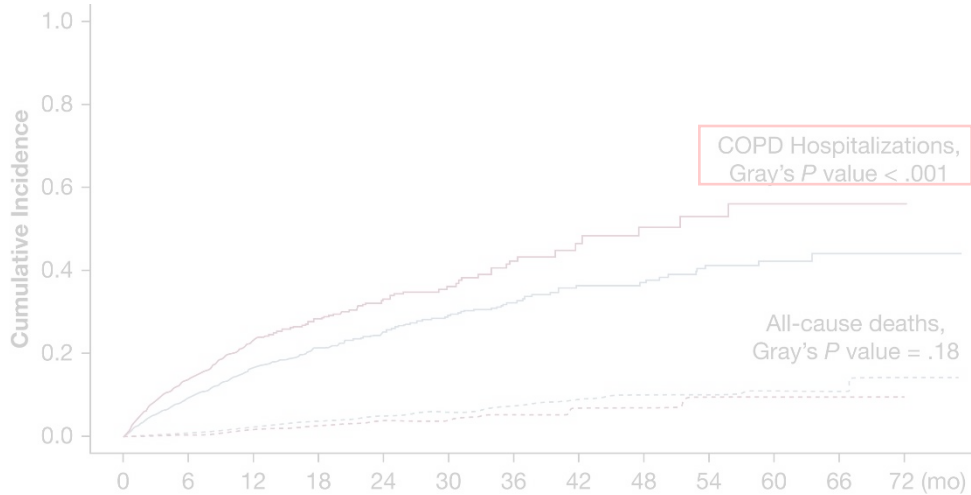


*Serum IgG Levels and Risk of COPD Hospitalization, Chest, 2020*

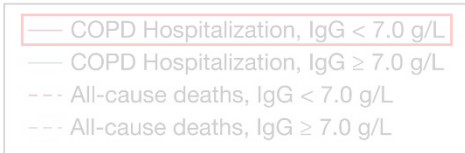
Serum IgG deficiency (<7g/L) is associated with morbidity in COPD.  
→ **whether concentrations in the lower end of the normal range?**



# Blood lab – Serum IgG



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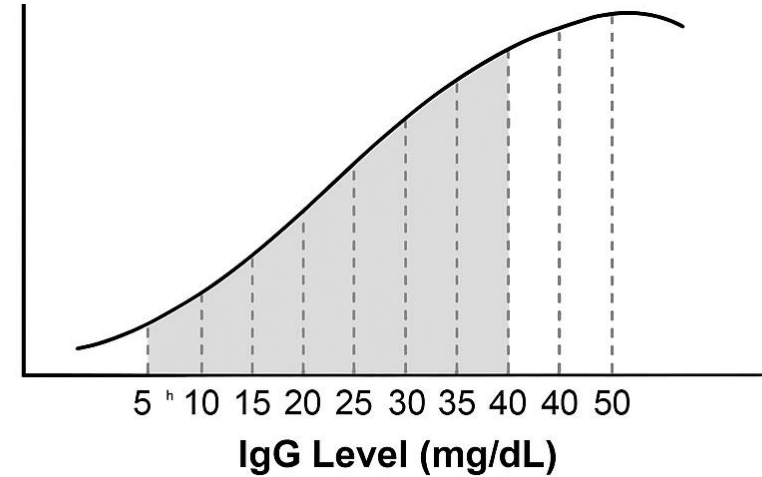
*Serum IgG Levels and Risk of COPD Hospitalization, Chest, 2020*

ORIG

Serum  
Exacerl

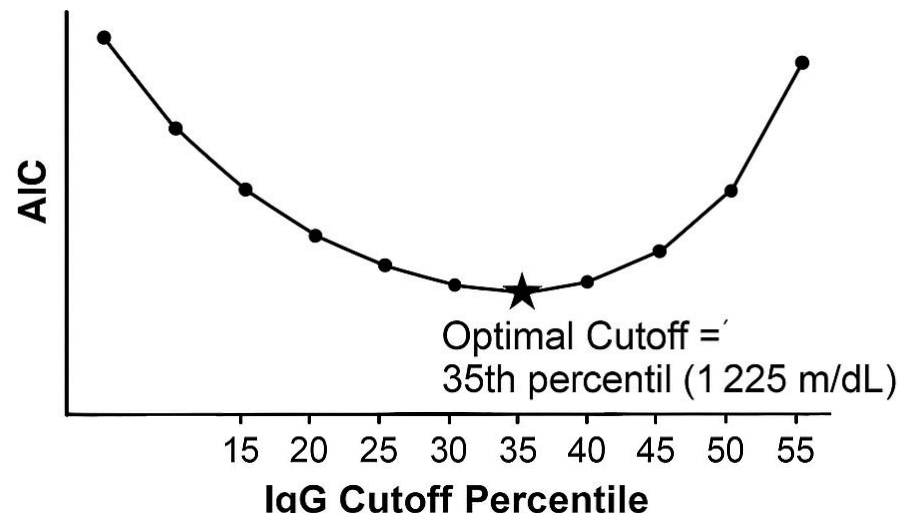
Michael Burr  
Martin Stamm  
Christopher  
David Coupe  
Fernando J.  
Mark Dransf

Population Density



Criner<sup>14</sup>,

B



- Met
- mult
- 40-8
- First
- Mea
- Prin
- Risk

## Statistical Methods - Cutoff value of IgG

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Serum IgG deficiency (<7g/L) is associated with morbidity in COPD.  
→ **whether concentrations in the lower end of the normal range?**



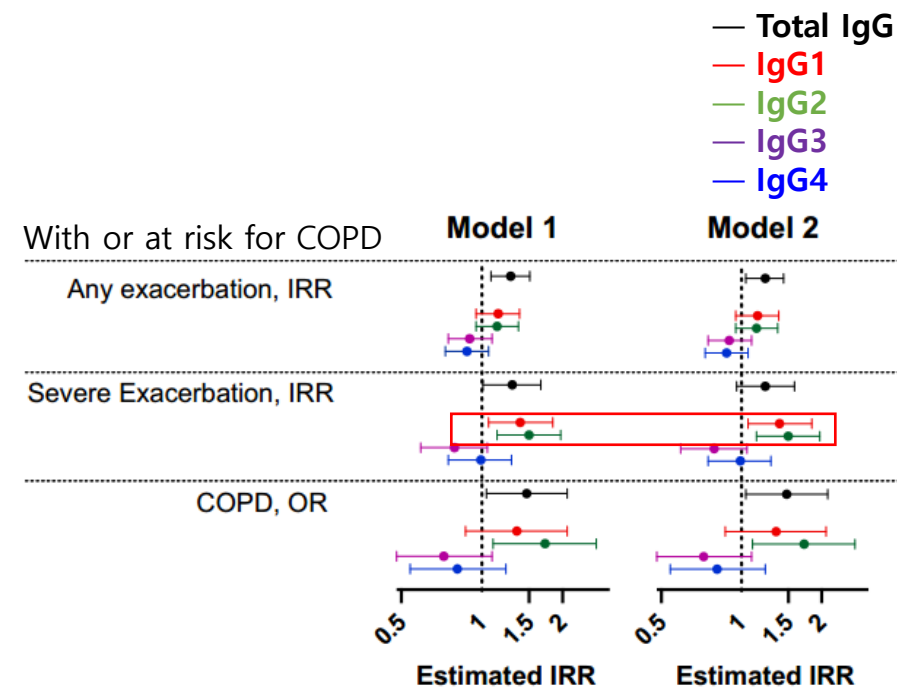
# Blood lab – Serum IgG

**Table 1.** Baseline Characteristics by Serum IgG Level Above or Below the 35th Percentile (1,225 mg/dl)

Characteristic	IgG ≤1,225 mg/dl (n=524)	IgG >1,225 mg/dl (n=973)	P Value
Median (IQR) total serum IgG, mg/dl	1,032 (900–1,133)	1,499 (1,377–1,594)	—
Spirometry-confirmed COPD	384 (73.4%)	642 (66.0%)	0.003
Age, yr	64.8 ± 8.6	64.4 ± 8.8	0.46
Female sex	243 (46.4%)	427 (43.9%)	0.36
White race	462 (88.7%)	720 (74.6%)	<0.001
Current smoker	191 (37.0%)	366 (38.2%)	0.66
Pack-years	52.3 ± 25.3	48.7 ± 22.5	0.004
History of occupational exposures	259 (49.9%)	492 (51.1%)	0.65
Education beyond high school	321 (61.4%)	538 (55.6%)	0.03
BMI, kg/m <sup>2</sup>	27.5 ± 5.2	28.1 ± 5.3	0.04
ICS use	207 (40.0%)	326 (34.0%)	0.02
SGRQ score	33.1 ± 20.6	32.1 ± 20.1	0.38
FEV <sub>1</sub> , % predicted	71.7 ± 26.4	73.3 ± 25.7	0.15
Any exacerbations in past year	141 (27.4%)	222 (23.1%)	0.07
Any severe exacerbations in past year	61 (11.9%)	103 (10.8%)	0.52

**Table 2.** Association of IgG Below the 35th Percentile or 1,225 mg/dl with Prospective Exacerbations and Prevalent Airflow Obstruction Consistent with COPD

	Model 1			Model 2		
	Coefficient	95% CI	P Value	Coefficient	95% CI	P Value
+ history of Exacerbation						
With or at risk for COPD (n=1,400)						
IRR for any exacerbation	1.28	1.08–1.51	0.004	1.23	1.04–1.44	0.01
IRR for severe exacerbation	1.30	1.01–1.66	0.04	1.23	0.96–1.58	0.10
OR for COPD	1.47	1.04–2.08	0.03	1.48	1.04–2.11	0.03
With airflow obstruction consistent with COPD (n=979)						
IRR for any exacerbation	1.22	1.02–1.46	0.03	1.19	1.02–1.42	0.047
IRR for severe exacerbation	1.20	0.93–1.56	0.16	1.17	0.90–1.52	0.24



Low serum IgG concentration is an independent factor for prevalent COPD and the risk of exacerbations among ever-smokers.



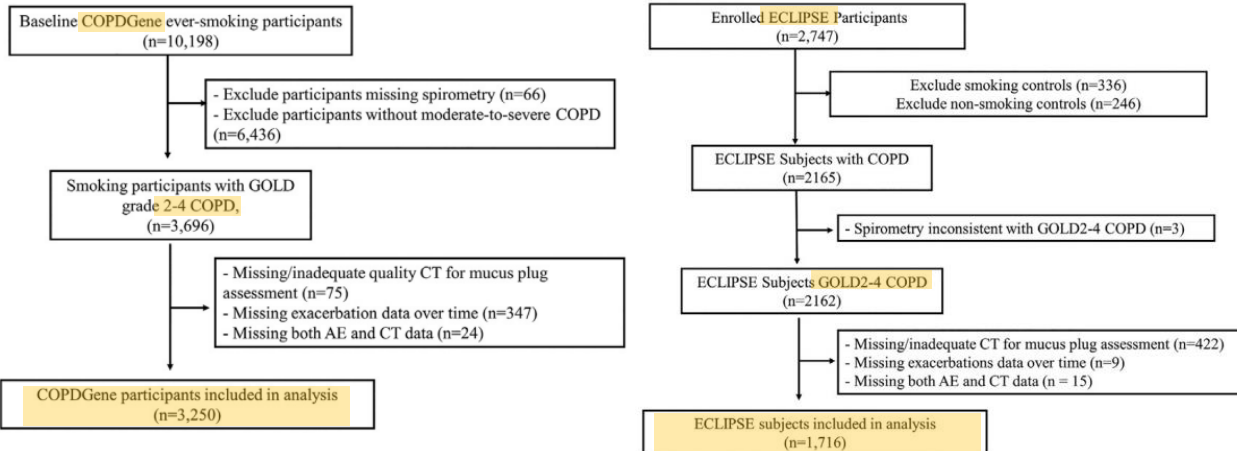
# CT images – Airway mucus plug

ORIGINAL ARTICLE

AJRCCM, 2025/05

## Airway Mucus Plugs on Chest Computed Tomography Are Associated with Exacerbations in Chronic Obstructive Pulmonary Disease

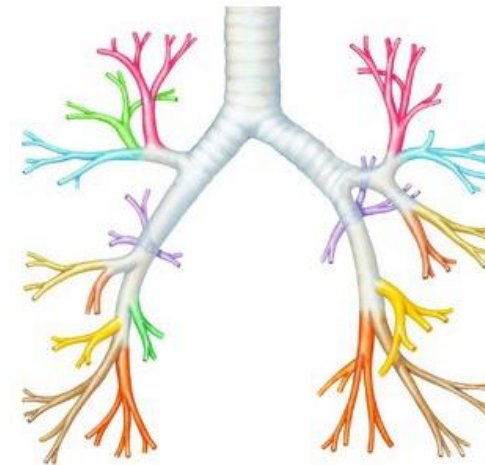
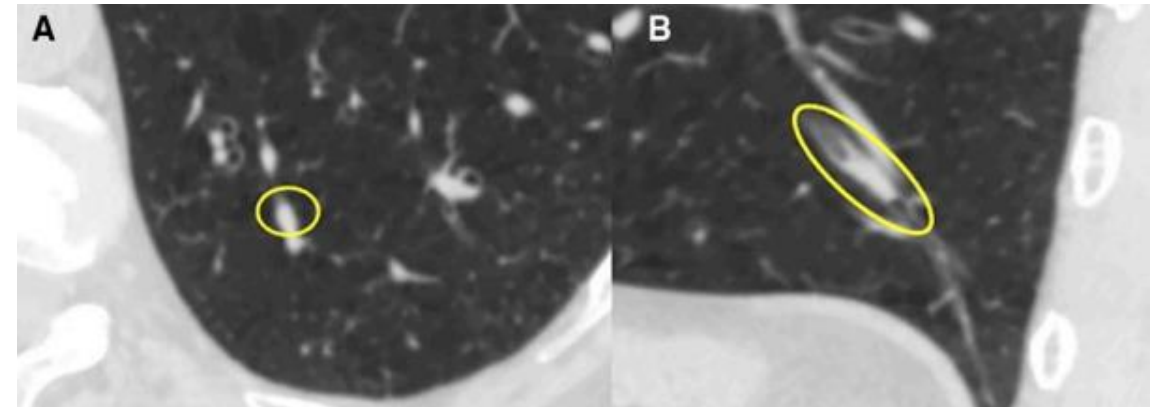
Emily Wan<sup>1,5,6</sup>, Andrew Yen<sup>7</sup>, Rim Elalami<sup>2</sup>, Scott Grumley<sup>8</sup>, Hrudaya P. Nath<sup>8</sup>, Wei Wang<sup>3,6</sup>, Sharon Brouha<sup>7</sup>, Padma P. Manapragada<sup>8</sup>, Mostafa Abozeed<sup>8</sup>, Muhammad Usman Aziz<sup>8</sup>, Mohd Zahid<sup>8</sup>, Asmaa N. Ahmed<sup>8</sup>, Nina L. Terry<sup>8</sup>, Pietro Nardelli<sup>4,6</sup>, James C. Ross<sup>4,6</sup>, Victor Kim<sup>9</sup>, Sushilkumar Sonavane<sup>10</sup>, Seth J. Kligerman<sup>11</sup>, Jørgen Vestbo<sup>12</sup>, Alvar Agustí<sup>13,14,15,16</sup>, Kangjin Kim<sup>1</sup>, Raúl San José Estépar<sup>4,6</sup>, Edwin K. Silverman<sup>1,2,6</sup>, Michael H. Cho<sup>1,2,6</sup>, and Alejandro A. Diaz<sup>2,6</sup>



<p>Multicenter observational prospective study (2007/11~2011/4) United states based 45-80yrs ≥10-pack-year smoking history Exacerbation assessed biannually</p>	<p>3year multicenter observational study 12 countries (multinational) 40-75yr ≥10-pack-year smoking history Exacerbation assessed monthly</p>
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### • CT Assessment

Mucus plugs were identified on **baseline non enhance chest CT**



- 18 bronchopulmonary segments
- Medium to large sized airways (2–10mm lumen diameter)
- completely occluded the lumen of an airway



# CT images – Airway mucus plug

**Table 1.** Baseline Characteristics by Cohort

Characteristic	COPDGene (N = 3,250)	ECLIPSE (N = 1,716)
Age, yr	63.7 ± 8.4	63.3 ± 7.1
Sex		
Male	1,784 (54.9%)	1,094 (63.7%)
Female	1,466 (45.1%)	622 (36.2%)
European ancestry	2,580 (79.4%)	1,680 (97.9%)
BMI	28.2 ± 6.2	26.4 ± 5.6
Current smoker	1,245 (38.3%)	638 (37.2%)
Pack-years of smoking	52.9 ± 27.2	49.1 ± 27.3
Exacerbation in 1 yr before enrollment	1,257 (38.7%)	782 (45.6%)
Chronic bronchitis	894 (27.5%)	560 (32.6%)
FEV <sub>1</sub> , L	1.45 ± 0.62	1.34 ± 0.52
FEV <sub>1</sub> , % predicted	50.6 ± 17.8	48.3 ± 15.8
Percent emphysema on CT*	13.5 ± 12.9	17.8 ± 12.1
Pi10 <sup>†</sup> (Airway wall thickness)	2.73 ± 0.56	3.95 ± 0.20
Years of follow-up	8.1 ± 4.3	2.7 ± 0.7
Total prospective acute exacerbations	4.9 ± 7.4	3.4 ± 3.8
Mucus plug score	1.4 ± 2.5	1.6 ± 2.6

• **Outcome**

- Primary outcome : Total number of AE
- Secondary outcome : Severe AE

**Table 2.** Association between Ordinal Mucus Plug Score Groups and AEs

	COPDGene			ECLIPSE		
	0	1-2	≥3	0	1-2	≥3
No. of patients	1,808	753	689	926	373	417
Moderate to severe AEs	Ref.	1.070 (1.048–1.093)	1.145 (1.098–1.195)	Ref.	1.056 (1.019–1.094)	1.115 (1.039–1.197)
Severe AEs	Ref.	1.045 (1.008–1.084)	1.092 (1.016–1.175)	Ref.	1.169 (1.072–1.273)	1.365 (1.15–1.622)

Mucus Plug Score (number of lung segments with mucus plugs)	COPDGene		ECLIPSE	
<b>Continuous</b>	Mucus plug가 1개 증가할 때 마다 exacerbation risk 가 3%증가 (dose response relationship)			
n	3,250		1,716	
Moderate-to-Severe AEs	1.025 [1.019-1.032]		1.027 [1.017-1.037]	
Severe AEs	1.022 [1.010-1.033]		1.054 [1.031-1.078]	
<b>Binary Groups</b>	<b>0</b>	<b>&gt;0</b>	<b>0</b>	<b>&gt;0</b>
n	1,808	1442	926	790
Moderate-to-Severe AEs	ref	1.108 [1.070-1.146]	ref	1.078 [1.017-1.376]
Severe AEs	ref	1.074 [1.013-1.14]	ref	1.411 [1.214-1.641]

CT-based mucus plugs represent an independent risk factor for AEs. This highlights the critical role of mucus clearance.



# CT images – Emphysema on CT

[ COPD Original Research ]



## Clinical and Prognostic Differences in Mild to Moderate COPD With and Without Emphysema

Check for updates

Huajing Yang, MD; Yuqiong Yang, MD, PhD; Fengyan Wang, MD, PhD; Chengyu Miao, MD; Zizheng Chen, MD; Shanshan Zha, MD; Xueping Li, MD; Jiawei Chen, MD; Aiqi Song, MD; Rongchang Chen, MD, PhD; and Zhenyu Liang, MD, PhD

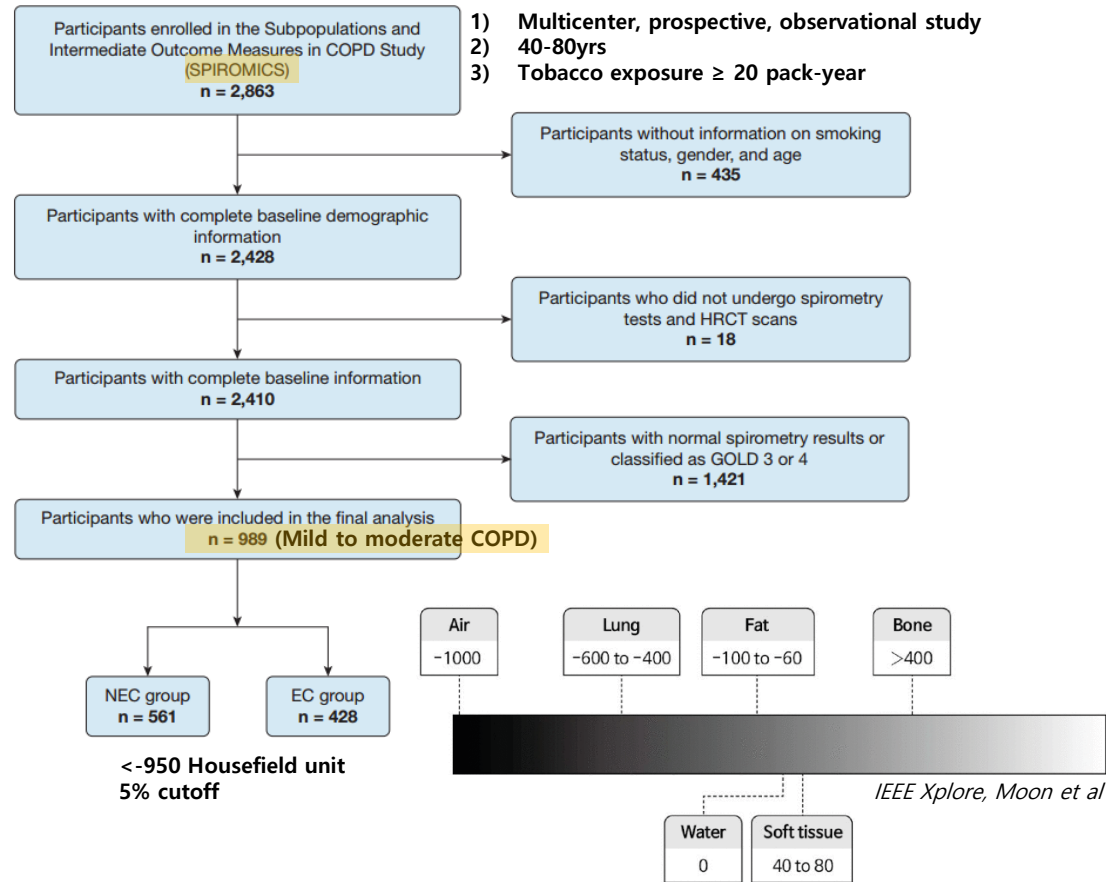


TABLE 2 ] Estimated Rates of Decline of FEV<sub>1</sub> Between Patients With Mild-to-Moderate COPD With and Without Radiographic Emphysema

Characteristic (n = 1,916)	Mild-to-Moderate COPD	
	Without Emphysema	With Emphysema
No. of participants at baseline	561	428
No. of participants at visit 4 (n = 484)	202	157
Observation time, median (interquartile range), y	2.01 (1.03-3.01)	2.07 (1.03-3.03)
FEV <sub>1</sub> , mean [SD], L		
At baseline	2.19 [0.64]	2.09 [0.65]
At visit 4	2.12 [0.62]	1.93 [0.68]
Unadjusted FEV <sub>1</sub> rate of decline (95% CI), mL/y <sup>a</sup>	-46.8 (-54.3 to -39.2)	-55.6 (-64.1 to -47.1)
Model 1 <sup>b</sup> 기본 인구통계학적 변수 보정	-46.9 (-54.5 to -39.3)	-56.1 (-64.5 to -47.6)
Model 2 <sup>c</sup> 폐/기도구조지표 추가변수 보정	-46.9 (-54.5 to -39.3)	-55.9 (-64.4 to -47.4)
FEV <sub>1</sub> rate of decline among those with active tobacco use (95% CI), mL/y <sup>a</sup>		
Model 1 <sup>b</sup>	-61.1 (-74.4 to -47.7)	-84.0 (-103.5 to -64.5)
Model 2 <sup>c</sup>	-61.2 (-74.5 to -47.8)	-83.8 (-103.2 to -64.3)
FEV <sub>1</sub> rate of decline among those who do not smoke (95% CI), mL/y <sup>a</sup>		
Model 1 <sup>b</sup>	-45.8 (-54.3 to -37.2)	-37.3 (-46.8 to -27.9)
Model 2 <sup>c</sup>	-37.3 (-46.8 to -27.9)	-44.6 (-54.0 to -35.2)
Acute COPD exacerbation (n = 1,916)		
Per person-year	0.25	0.36
Total No.	614	697
Severe acute COPD exacerbation		
Per person-year	0.08	0.10
Total No.	209	203

e-Table 1. Estimated Difference in Rates of FEV<sub>1</sub> mL/year Decline among the groups<sup>a</sup>

	Diff, (95%CI) <sup>d</sup>	P value	q value
EC group vs. NEC group			
Unadjusted	-8.8 (-23.7, 6.1)	0.428	0.476
Model 1 <sup>b</sup>	-9.1 (-24.0, 5.7)	0.391	0.466
Model 2 <sup>c</sup>	-9.0 (-23.9, 5.9)	0.404	0.466
Currently smoking vs. Not Currently smoking			
Unadjusted	-25.4 (-37.6, -13.2)	<.001	<.001
Model 1 <sup>b</sup>	-25.4 (-37.6, -13.3)	<.001	<.001
Model 2 <sup>c</sup>	-25.5 (-37.7, -13.4)	<.001	<.001



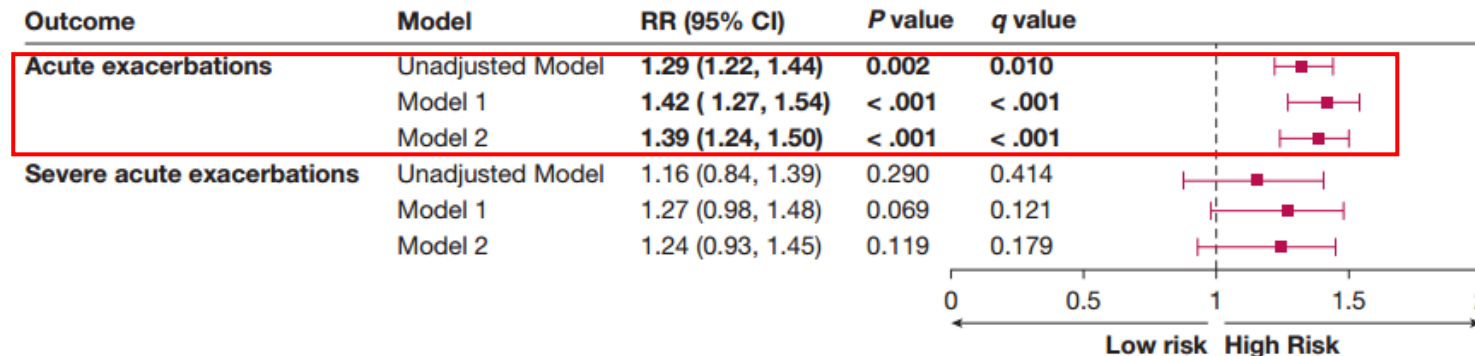
# CT images – Emphysema on CT

**e-Table 2.** Annual Change in COPD Symptom Scores and Six-Minute Walk Distance in Units Per Year<sup>a</sup>

COPD Outcome (n=1916)	Mild-to-moderate COPD	
	Without emphysema Rate (95% CI) <sup>d</sup>	With emphysema Rate (95% CI) <sup>d</sup>
<b>Unadjusted Model</b>		
COPD Assessment Test Score	-0.2 (-0.4, 0.0)	0.3 (0.0, 0.5)
St. George' Respiratory Score	-0.2 (-0.6, 0.1)	0.7 (0.3, 1.1)
mMRC Score	0.0 (-0.0, 0.1)	0.1 (0.1, 0.1)
Six-minute Walk Distance	-9 (-12, -6)	-12 (-16, -9)
<b>Model 1<sup>b</sup></b>		
COPD Assessment Test Score	-0.1 (-0.4, 0.1)	0.3 (0.0, 0.5)
St. George' Respiratory Score	-0.2 (-0.5, 0.2)	0.7 (0.3, 1.1)
mMRC Score	0.0 (0.0, 0.1)	0.1 (0.1, 0.1)
Six-minute Walk Distance	-9 (-12, -6)	-12 (-16, -9)
<b>Model 2<sup>c</sup></b>		
COPD Assessment Test Score	-0.1 (-0.3, 0.1)	0.3 (0.0, 0.5)
St. George' Respiratory Score	-0.1 (-0.5, 0.2)	0.7 (0.3, 1.1)
mMRC Score	0.0 (0.0, 0.1)	0.1 (0.1, 0.1)
Six-minute Walk Distance	-9 (-12, -6)	-12 (-16, -9)

**TABLE 4 ]** Estimated Differences in Rates of Change in COPD Outcomes Between Groups<sup>a</sup>

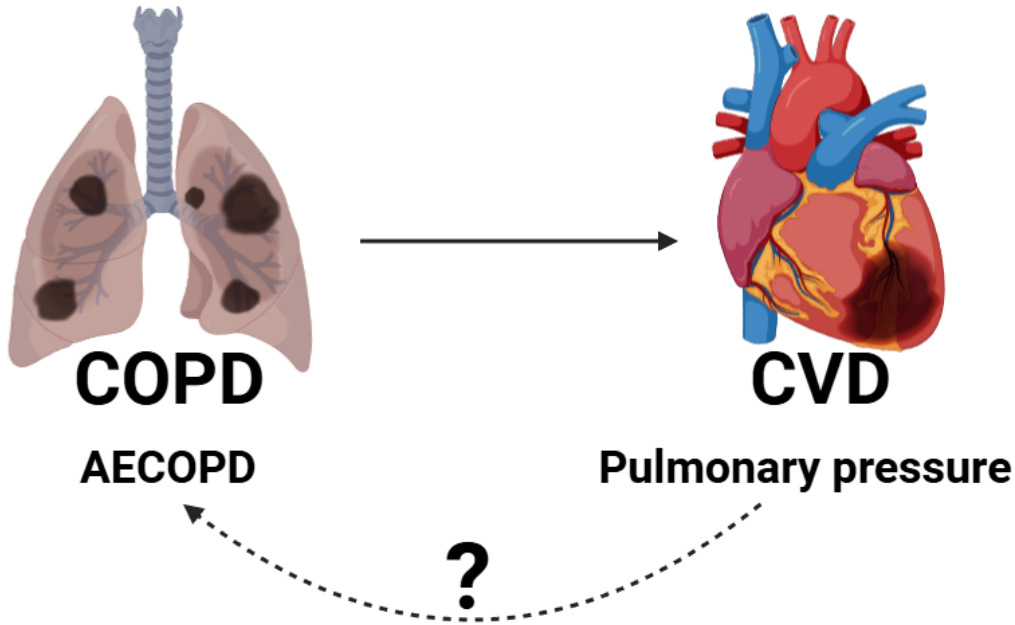
COPD Outcome	EC Group vs NEC Group		q Value
	Difference (95% CI) <sup>b</sup>	P Value	
<b>Unadjusted model</b>			
COPD Assessment Test score	0.5 (0.0 to 0.9)	<b>.029</b>	0.067
SGRQ score	1.0 (0.2 to 1.7)	<b>.005</b>	<b>0.019</b>
mMRC score	0.1 (0.0 to 0.1)	<b>.004</b>	<b>0.017</b>
6-min walk distance	-3 (-9 to 3)	.484	0.484
<b>Model 1<sup>c</sup></b>			
COPD Assessment Test score	0.4 (-0.0 to 0.8)	.077	0.128
SGRQ score	0.9 (0.2 to 1.6)	<b>.010</b>	<b>0.030</b>
mMRC score	0.1 (0.0 to 0.1)	<b>.011</b>	<b>0.030</b>
6-min walk distance	-3 (-9 to 2)	.452	0.484
<b>Model 2<sup>d</sup></b>			
COPD Assessment Test score	0.4 (-0.0, 0.8)	.083	0.131
SGRQ score	0.9 (0.1, 1.6)	<b>.012</b>	<b>0.030</b>
mMRC score	0.1 (0.0, 0.1)	<b>.008</b>	<b>0.027</b>
6-min walk distance	-3 (-9, 3)	.470	0.128



But, EC group had 1) worse health-related quality of life and 2) a higher rate of acute respiratory exacerbations compared with NEC.



# Pulmonary Pressure



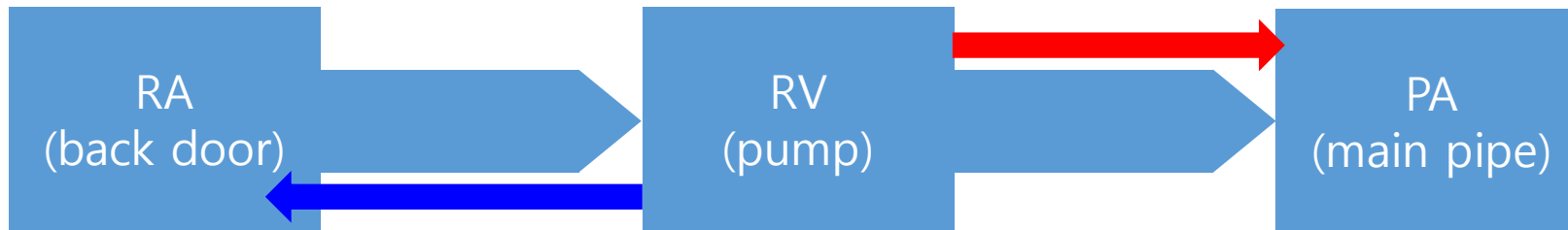
EUROPEAN RESPIRATORY JOURNAL  
ORIGINAL RESEARCH ARTICLE  
E. RASTODER ET AL.

## Pulmonary pressure increases during acute exacerbation in COPD and clinical outcome

Ema Rastoder<sup>1,16</sup>, Pradeesh Sivapalan<sup>1,2,16</sup>, Caroline Hedsund<sup>1</sup>, Peter Kamstrup<sup>1</sup>, Tor Biering-Sørensen<sup>3,4,5,6</sup>, Maria Dons<sup>3,4</sup>, Trine Charlotte Bistrup Petersen<sup>3,4</sup>, Filip Soeskov Davidovski<sup>3,4</sup>, Kristoffer Grundtvig Skaarup<sup>3,4</sup>, Morten Sengeløv<sup>3,4</sup>, Emil Durukan<sup>3,4</sup>, Ditte Vesterlev<sup>3,4</sup>, Helena Zander Wodschow<sup>7</sup>, Lars Pedersen<sup>8</sup>, Josefin Eklöf<sup>1</sup>, Anna Kubel Vogensen<sup>1</sup>, Mia Moberg<sup>9</sup>, Julie Janner<sup>9</sup>, Louise Lindhardt Toennesen<sup>9</sup>, Hashmat S.Z. Bahrami<sup>10,11</sup>, Ulrik Dixen<sup>10</sup>, Jens Dahlgaard Hove<sup>10</sup>, Magnus Thorsten Jensen<sup>6</sup>, Daniel Alexander Ackermann<sup>1</sup>, Alexander Jordan<sup>1</sup>, Valdemar Rømer<sup>1</sup>, Søren Sperling<sup>12</sup>, Elisabeth Bendstrup<sup>12,13</sup>, Casper Falster<sup>14,15</sup>, Christian B. Laursen<sup>14,15</sup>, Jørn Carlsen<sup>2,5</sup> and Jens-Ulrik Stæhr Jensen<sup>1,2</sup>

- **Aim**
  - 1) Whether pulmonary pressures were elevated during hospitalization with AECOPD compared with the stable phase?
  - 2) Association between **TR gradient** and day alive and out of hospital (DAOH)

1. (폐동맥압 높은경우) RV 수축으로 압력이 올라가면

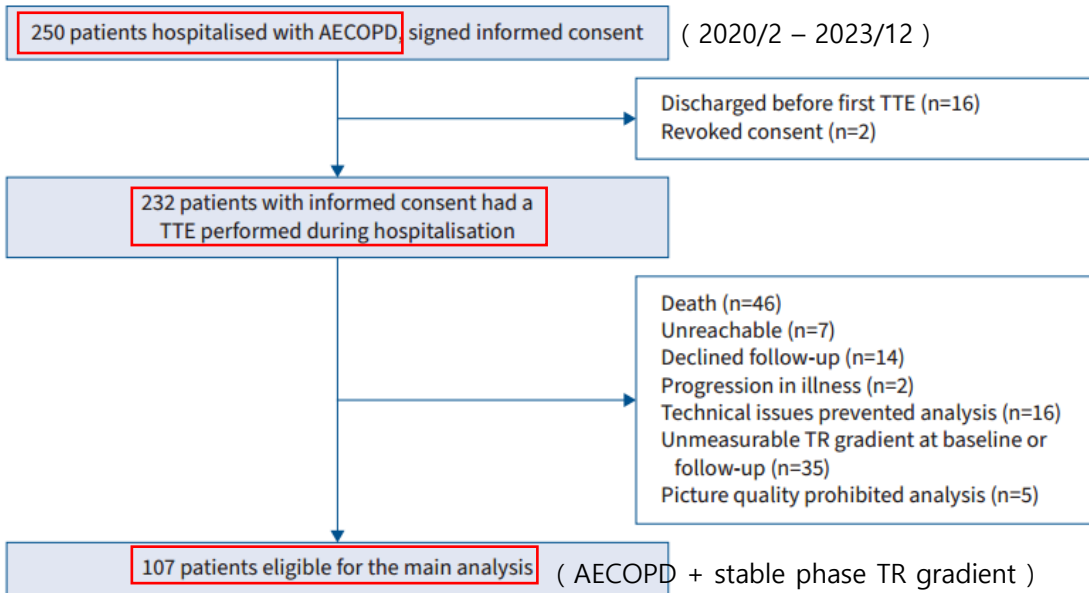


2. 일부 혈액이 삼첨판을 통해 우심방으로 이동  
RA와 RV사이 압력차가 크면 더 빠르게 역류 = TR gradient 올라감  
→ 따라서, TR gradient는 폐동맥압의 간접 지표



# Pulmonary Pressure

- Method
- 1) **COPD Exacerbation and Pulmonary hypertension study**
  - Multicenter prospective paired measurement study in Denmark
- 2) **Inclusive criteria**
  - COPD for GOLD
  - Inclusion within the first 72hr of hospitalization
- 3) **Stable phase**
  - Discharged for at least 1M following hospitalization from AECOPD



- **Primary Outcome**  
: TR gradient (mmHg)

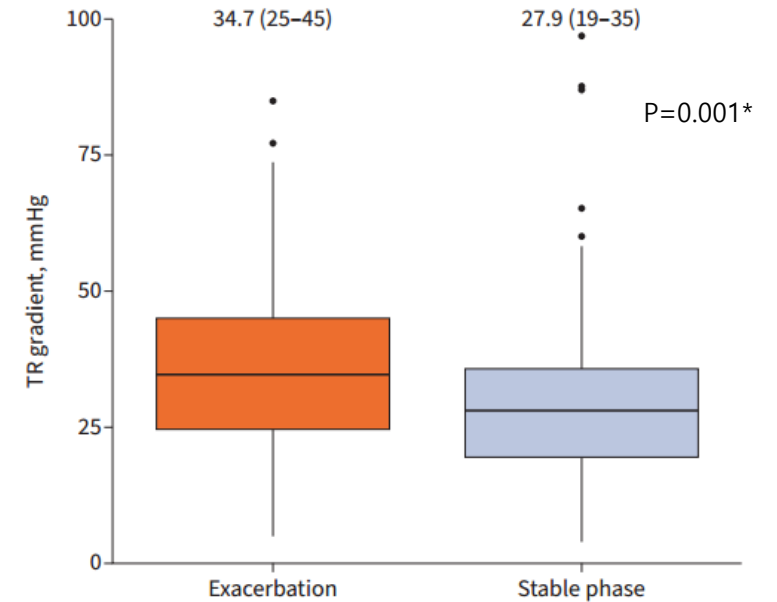


TABLE 2 Transthoracic echocardiography parameters of cardiac structure and function during acute exacerbation in COPD (AECOPD) and the stable phase

	AECOPD	Stable phase	Mean difference (95% CI)	p-value
RA area, cm <sup>2</sup>	16.5±5.7	15.7±5.7	0.7 (-0.35-1.77)	0.19
RV diameter, cm	3.7±0.7	3.5±0.8	0.2 (-0.00-0.33)	0.06
LV diameter, cm	4.5±0.9	4.4±0.9	0.0 (-0.10-0.16)	0.56
Interventricular septum, cm	1.2±0.3	1.2±0.3	0.0 (-0.05-0.07)	0.80
LV/RV ratio	0.6±0.4	0.6±0.4	0.0 (-0.06-0.11)	0.57
TAPSE, cm	2.1±0.6	2.2±0.5	0.0 (-0.13-0.12)	0.85
TR gradient, mmHg	35.7±16.0	29.7±16.6	6.0 (2.5-9.6)	0.001
RAP, mmHg	6.9±4.2	6.0±3.6	0.9 (-0.1-1.8)	0.009
PSAP, mmHg	41.4±16.6	33.9±17.4	7.6 (3.4-11.7)	0.001
PSAP/TAPSE ratio	2.0±0.9	1.6±0.8	0.5 (0.2-0.7)	0.000

AECOPD에서 증가하는 폐혈관 저항의 경우 일시적으로 증가, RV size 등과 같은 구조적 지표의 변화까지는 즉시 반영되지 않음

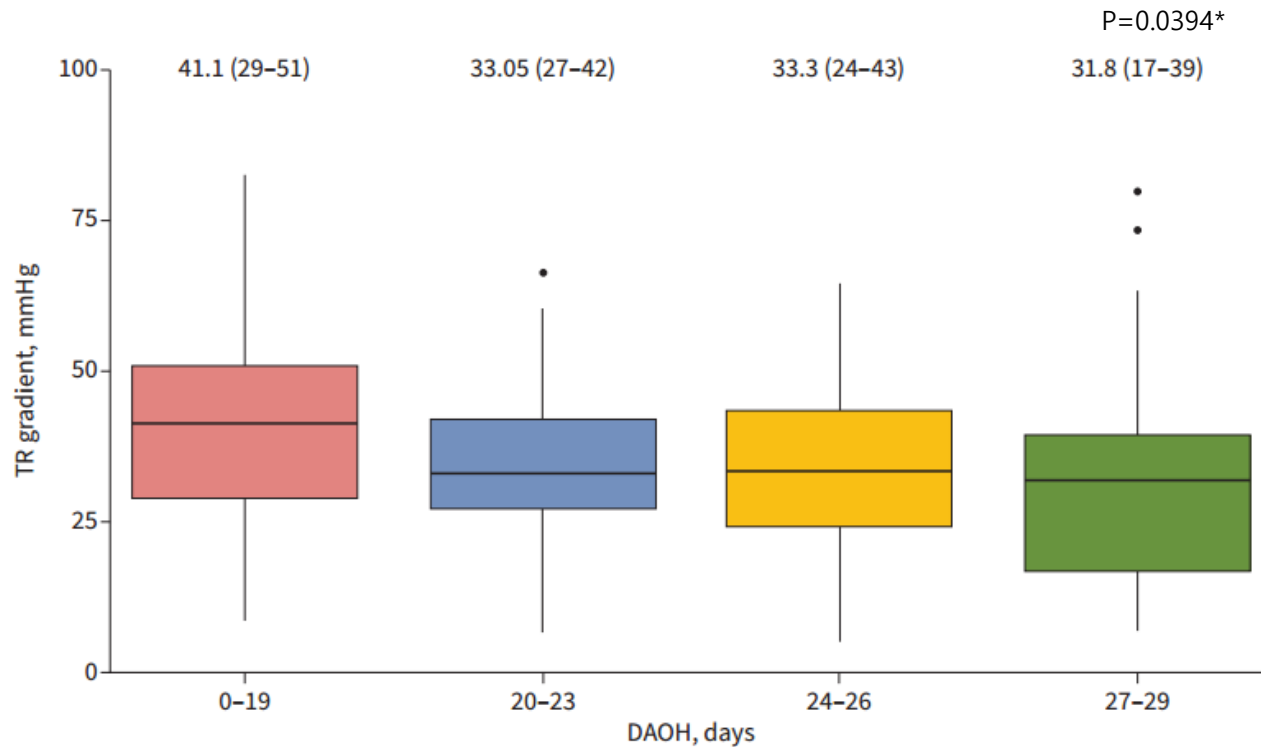


# Pulmonary Pressure

- **Secondary analysis :**

Out of the 232 participants with an index TTE,

**158 had a measurable TR gradient during AECOPD** and available data to measure **DAOH (Day alive and out of hospital)**



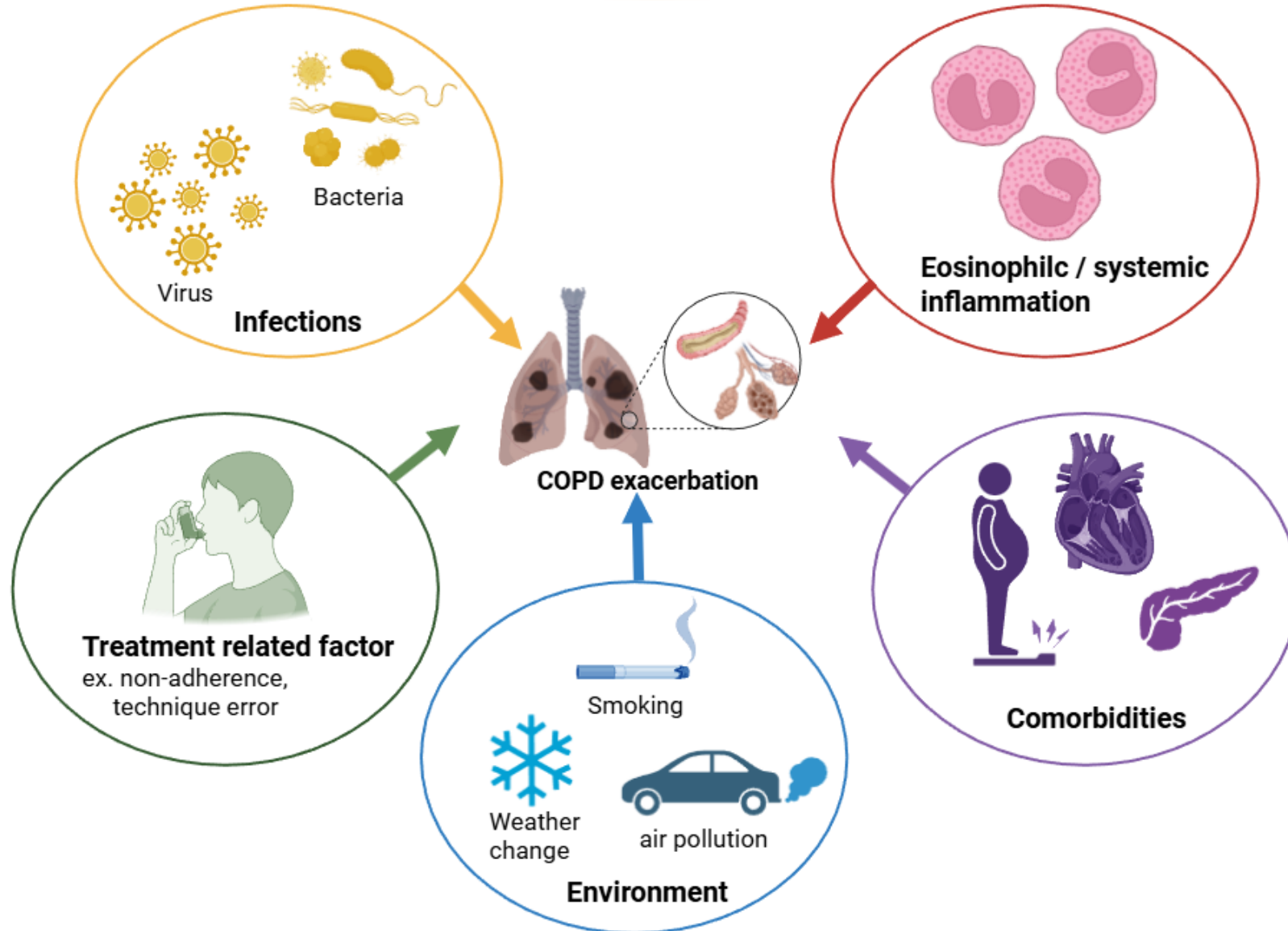
**Table A2.** TR gradient and RA area, and length of hospitalization.

	Length of hospitalization		
	Normal level Median (IQR)	Higher level Median (IQR)	P-Value (Wilcoxon-test)
TR gradient	4 (3,6) days	7 (4,9) days	0.005**
RV area	5 (3,7) days	5 (3,11) days	0.34

Further research is needed whether elevated pulmonary pressures contribute to exacerbation development and DAOH or are simply a consequence of the acute exacerbation phase.



# COPD exacerbation의 원인





# COPD exacerbation의 원인 - Infection

Original Article



## Clinical Significance of Various Pathogens Identified in Patients Experiencing Acute Exacerbations of COPD: A Multi-center Study in South Korea

Hyun Woo Ji, M.D.<sup>1\*</sup>, Soojoung Yu, M.D.<sup>2</sup>, Yun Su Sim, M.D., Ph.D.<sup>3</sup>, Hyewon Seo, M.D.<sup>4</sup>, Jeong-Woong Park, M.D., Ph.D.<sup>5</sup>, Kyung Hoon Min, M.D., Ph.D.<sup>6</sup>, Deog Kyeom Kim, M.D., Ph.D.<sup>7</sup>, Hyun Woo Lee, M.D.<sup>7</sup>, Chin Kook Rhee, M.D., Ph.D.<sup>8</sup>, Yong Bum Park, M.D., Ph.D.<sup>9</sup>, Kyeong-Cheol Shin, M.D., Ph.D.<sup>10</sup>, Kwang Ha Yoo, M.D., Ph.D.<sup>11</sup> and Ji Ye Jung, M.D., Ph.D.<sup>10</sup>

**Supplementary Table S1.** The proportions of each specimen type and microbiological evaluation method

Variable	Total (n=1,108)
<b>Specimen</b>	
Sputum	1,092 (98.6)
Bronchial washing	23 (2.1)
Nasopharyngeal swab	796 (71.8)
<b>Testing method</b>	
<b>Bacteria</b>	
Culture	1,092 (98.6)
Atypical PCR	613 (55.3)
IgM ELISA	701 (63.3)
<b>Virus</b>	
PCR	927 (83.6)
Rapid antigen test	754 (68.1)

Group 4-5 sputum, predominant microorganism

Retrospective study, 28 hospitals in South Korea  
**1,186 patients** diagnosed with AECOPD from **January 2015 to December 2018**

### • Inclusion criteria

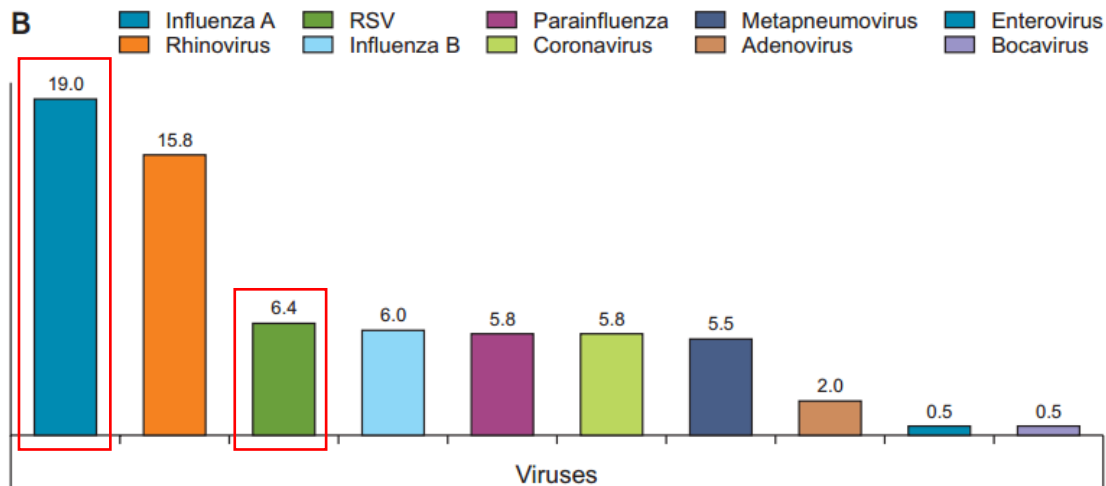
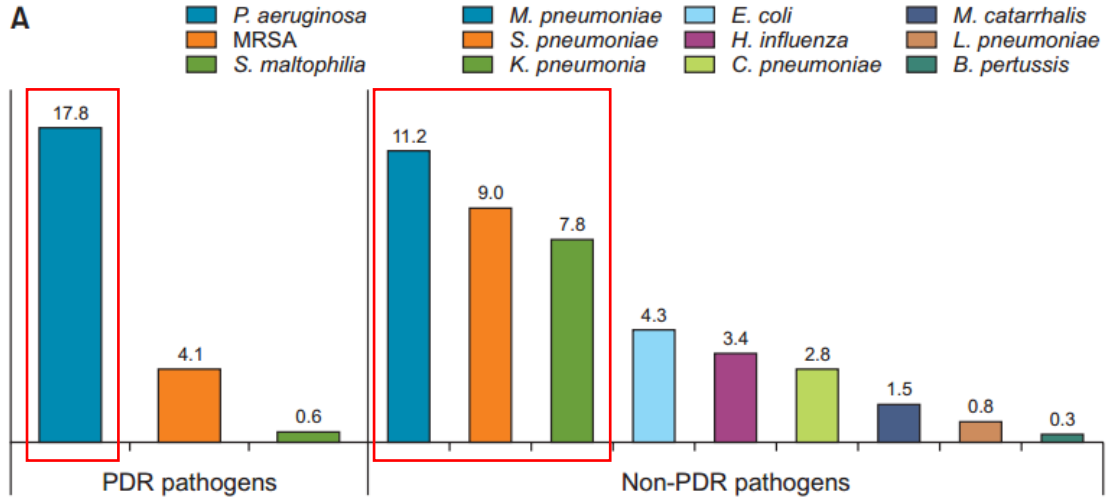
- (1) ≥40yrs and a history of COPD confirmed by PFT
- (2) diagnosis of moderate-to-severe AECOPD
- (3) assessment using all standard tests for pathogen detection  
 → conducted within 48hr following diagnosis of AECOPD

Characteristic	Total (n=1,186)
Age, yr	78.8±9.2
Male sex	979 (82.5)
Duration of COPD, yr	7.6±6.6
<b>Smoking history</b>	
Never smoked	313 (27.1)
Current smoker	156 (13.5)
Former smoker	688 (59.5)
Pack year	38.7±26.0
<b>Underlying respiratory disease</b>	
Tuberculosis	377 (31.8)
Bronchiectasis	169 (14.2)
Interstitial lung disease	27 (2.3)
<b>Comorbidities</b>	
Diabetes mellitus	318 (26.8)
Hypertension	584 (49.2)
Liver cirrhosis	23 (1.9)
Congestive heart failure	166 (14.0)
Chronic kidney disease	76 (6.4)
Cerebrovascular disease	70 (5.9)
Advanced cancer	138 (11.6)
FEV <sub>1</sub> , %	49.5±21.1

CAT score	22.5±9.8
mMRC	2.3±0.9
<b>During AECOPD</b>	
ICU administration	112 (9.5)
Hospital length of stay, day	12.6±13.7
Antibiotics use	1139 (95.8)
Unused	47 (4.2)
<b>Monotherapy</b>	
Beta-lactam	163 (57.8)
Quinolone	107 (37.9)
Macrolide	5 (1.8)
Others	7 (2.5)
<b>Dual combination</b>	
Beta-lactam+Quinolone	280 (43.0)
Beta-lactam+Macrolide	236 (36.3)
Beta-lactam+Others	31 (4.8)
Quinolone+Others	27 (4.1)
Macrolide+Others	19 (2.9)
<b>Triple combination</b>	
	128 (11.5)
<b>Levels of healthcare system</b>	
Secondary	396 (33.5)
Tertiary	709 (66.5)



# COPD exacerbation의 원인 - Infection



**Table 3.** Multivariate logistic analysis of the associated factors for infection with PDR pathogens during AECOPD

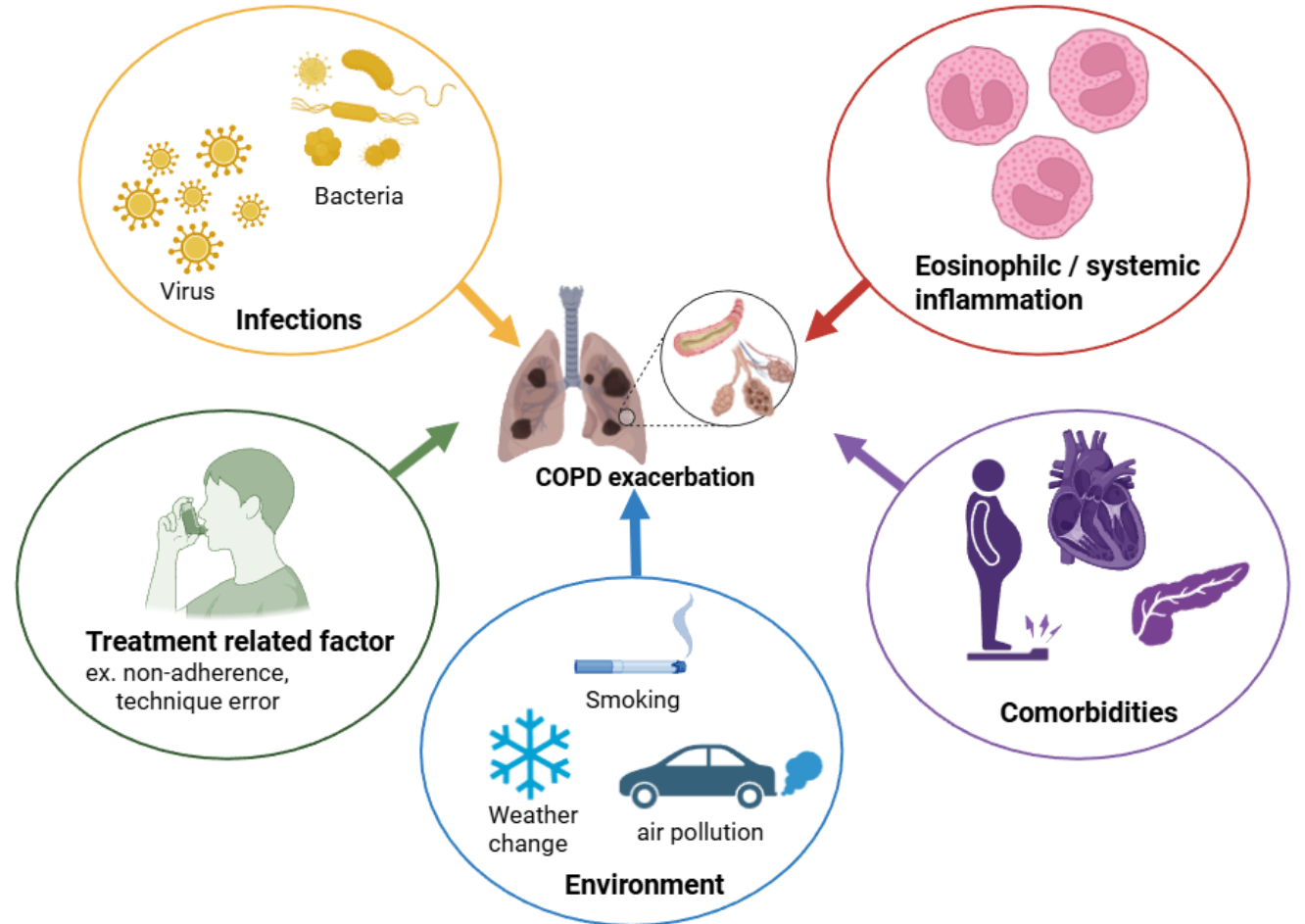
Associated factors	ICS model		Triple inhaler model	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age, yr	1.01 (0.98–1.03)	0.638	1.01 (0.98–1.04)	0.573
Male sex	1.41 (0.78–2.55)	0.261	1.50 (0.82–2.74)	0.189
BMI, kg/m <sup>2</sup>	0.97 (0.91–1.04)	0.405	0.97 (0.91–1.04)	0.355
FEV <sub>1</sub> >60%	0.74 (0.41–1.34)	0.319	0.79 (0.44–1.43)	0.435
<b>Comorbidities</b>				
Tuberculosis	1.66 (1.01–2.75)	0.046	1.64 (0.99–2.72)	0.054
Bronchiectasis	1.99 (1.06–3.75)	0.032	1.94 (1.02–3.67)	0.043
<b>Treatment status</b>				
Systemic steroids	1.47 (0.85–2.57)	0.172	1.45 (0.84–2.53)	0.186
ICS	1.62 (0.97–2.71)	0.066	NA	NA
Triple therapy	NA	NA	2.04 (1.24–3.35)	0.005

Systemic steroid를 사용한 것이 PDR infection 의 risk 를 증가시키지 않지만, ICS를 사용하는 것은 PDR infection의 risk를 높이는 경향성이 있구나!



# COPD exacerbation의 예방 & 치료

- (1) Vaccination : RSV, Covid-19
- (2) Eosinophil / systemic inflammation : biologics, anti-inflammatory agents
- (3) Treatment related factor
- (4) Comorbidities control





# COPD exacerbation의 예방/치료 - (1) Vaccination

Review

DOI: <https://doi.org/10.4046/trd.2025.0173> [Accepted]

Published online November 19, 2025.



## Expert Consensus Statement on the Disease Burden and Vaccination for Respiratory Syncytial Virus (RSV) Infection in Adults

Joon Young Choi<sup>1</sup>, Chin Kook Rhee<sup>2</sup>, Yong-Il Hwang<sup>3</sup>, Ji-Yong Moon<sup>4</sup>, Kwang Ha Yoo<sup>4</sup>, Hyoung Kyu Yoon<sup>5</sup>

**Table 3. Reported annual positive rate of respiratory viruses from 2015 to 2019 in Korean Influenza and Respiratory Surveillance System (KINRESS)**

Year	Rhinovirus	Adenovirus	Human coronavirus	Respiratory syncytial virus	Influenza virus	Parainfluenza virus	Human metapneumovirus	Human bocavirus
2015	31.4%	12.2%	3.0%	17.8%	11.7%	11.9%	6.2%	5.8%
2016	24.7%	16.6%	6.6%	17.7%	13.6%	9.2%	5.6%	6.0%
2017	29.8%	9.2%	5.3%	20.1%	12.1%	11.1%	6.1%	6.4%
2018	23.6%	12.4%	6.5%	14.8%	21.5%	9.7%	6.4%	5.0%
2019	29.3%	15.0%	4.3%	11.7%	13.8%	12.6%	6.9%	6.3%

**Severe RSV Requiring hospitalization in America (2022.10-2023.04)**



MDedge, 2024

**Table 4. Rates of RSV co infection with respiratory diseases in Korea**

Study	Study design	Disease	Age group	Respiratory Diseases/Total RSV cases (%)	RSV-related respiratory complications
<b>Proportion of respiratory diseases among adults with RSV</b>					
An TJ, et al. 2024 <sup>18</sup>	Multicenter, retrospective	AE-COPD, asthma	≥18 YOA	11/87 (12.6)	Asthma (≥18 YOA) COPD (≥40 YOA) 50/1,314 (3.4-5.0)
Lee HW, et al. 2022 <sup>24</sup>	Multicenter, observational	AE-COPD	≥40 YOA	3/87 (3.4)	≥40 YOA Mean age: 73.78±9.22 42/1,186 (3.5)
Kwon YS, et al. 2017 <sup>20</sup>	Retrospective	COPD	≥18 YOA	26/227 (11.5)	Median age: 70 YOA 28/214 (13.1)
		Asthma	≥18 YOA	15/227 (6.6)	
Park SY, et al. 2017 <sup>21</sup>	Single-center, retrospective	COPD	≥18 YOA	16/227 (7.0)	Mean age: 76.5±7.9 YOA 16/108 (14.8)
		Asthma	≥18 YOA		
		Others	≥18 YOA		
Seo KH, et al. 2017 <sup>26</sup>	Prospective	AE-asthma	≥18 YOA (Adult)		RSV: 11/323 (3.4) In exacerbated cases: 8/259 (11.8) In stable cases: 3/64 (25.0)
Kwak HJ, et al. 2016 <sup>27</sup>	Single-center, retrospective	AE-COPD	Mean age: 69.2±11.0 YOA		12/78 (14.1)

3~25% of COPD patients in RSV infection



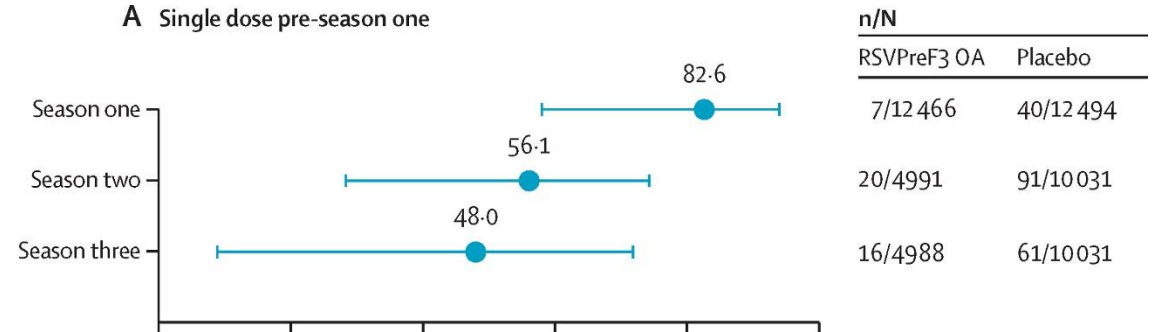
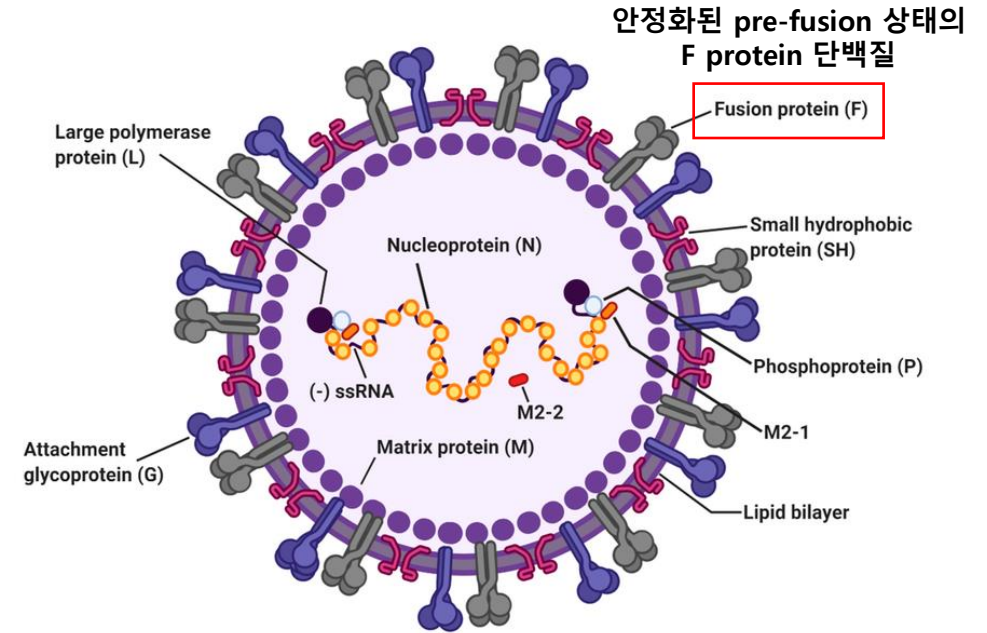
# COPD exacerbation의 예방/치료 – (1) Vaccination

## Vaccination for Stable COPD

Figure 3.6

People with COPD should receive all recommended vaccinations in line with the relevant local guidelines:

- Yearly influenza vaccination (**Evidence B**)
- SARS-CoV-2 (COVID-19) vaccination based on WHO and CDC updated recommendations (**Evidence B**)
- Either one dose of 21-valent pneumococcal conjugate vaccine (PCV21) or one dose PCV20, as recommended by the CDC (**Evidence B**). Pneumococcal vaccination has been shown to reduce the incidence of community-acquired pneumonia and exacerbations for people with COPD (**Evidence B**)
- Respiratory syncytial virus (RSV) vaccination for individuals aged  $\geq 60$  years and/or with chronic heart or lung disease, as recommended by the CDC (**Evidence A**)
- Tdap (dTdap/dTPa) vaccination to protect against pertussis (whooping cough) for people with COPD that were not vaccinated in adolescence, as recommended by the CDC (**Evidence B**)
- Zoster vaccine to protect against shingles for people with COPD aged  $> 50$  years, as recommended by the CDC (**Evidence B**)



Lancet, 2025



# COPD exacerbation의 예방/치료 - (1) Vaccination

Original Article



## Effects of Vaccination on Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Nationwide Population-Based Cohort Study

Sang Hyuk Kim<sup>1,2\*</sup>, Hyun Lee<sup>3\*</sup>, Min Ji Kim<sup>4,5</sup>, Min Gu Kang<sup>4,5</sup>, Jong Seung Kim<sup>4,5,6</sup>, Jong Geol Jang<sup>7</sup>, Youlim Kim<sup>8</sup>, Hyeon-Kyoung Koo<sup>9</sup>, Chin Kook Rhee<sup>10</sup>, Kyung Hoon Min<sup>2</sup>, Yong Il Hwang<sup>11</sup>, Deog Kyeom Kim<sup>12</sup>, Yong Bum Park<sup>13</sup>, Ji-Yong Moon<sup>8</sup> and on Behalf of the Korean COPD Study Group

Excluded:  
 No health examination data (n=4,713,157)  
 Vaccination after COVID-19 (n=810)  
 COPD diagnosis after COVID-19 (n=71)  
 Death before index date or December 31, 2021 (n=4,004)

- \* Inclusion criteria
- 1) ≥20yrs
  - 2) Dx COPD before 2021/2/26
  - 3) COV19 infection before 2022/3/31

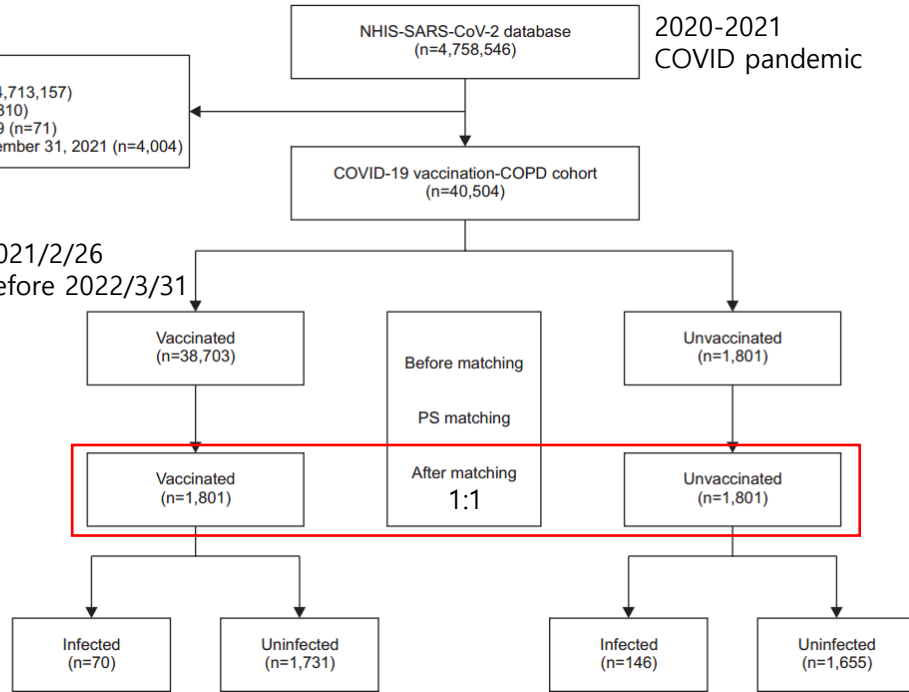


Table 2. Risk of AECOPD based on COVID-19 vaccination status

COVID-19 vaccination	Number	Number of AECOPD	AECOPD, /10,000 population	HR (95% CI)
No	1,801	144	3,410	Reference
Yes	1,801	73	1,683	0.55 (0.41–0.72)

Figure 2. Kaplan-Meier curves for acute exacerbation of chronic obstructive pulmonary disease (AECOPD) based on coronavirus disease 2019 (COVID-19) vaccination status.

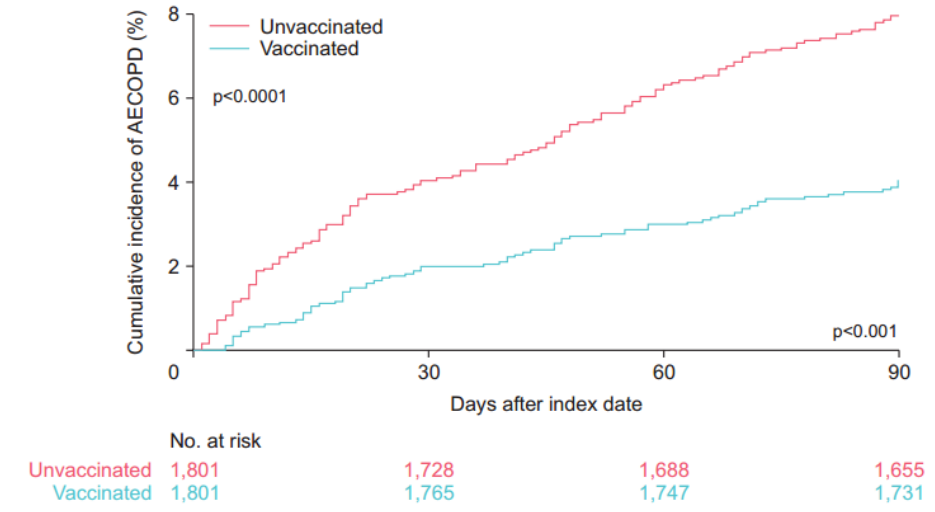
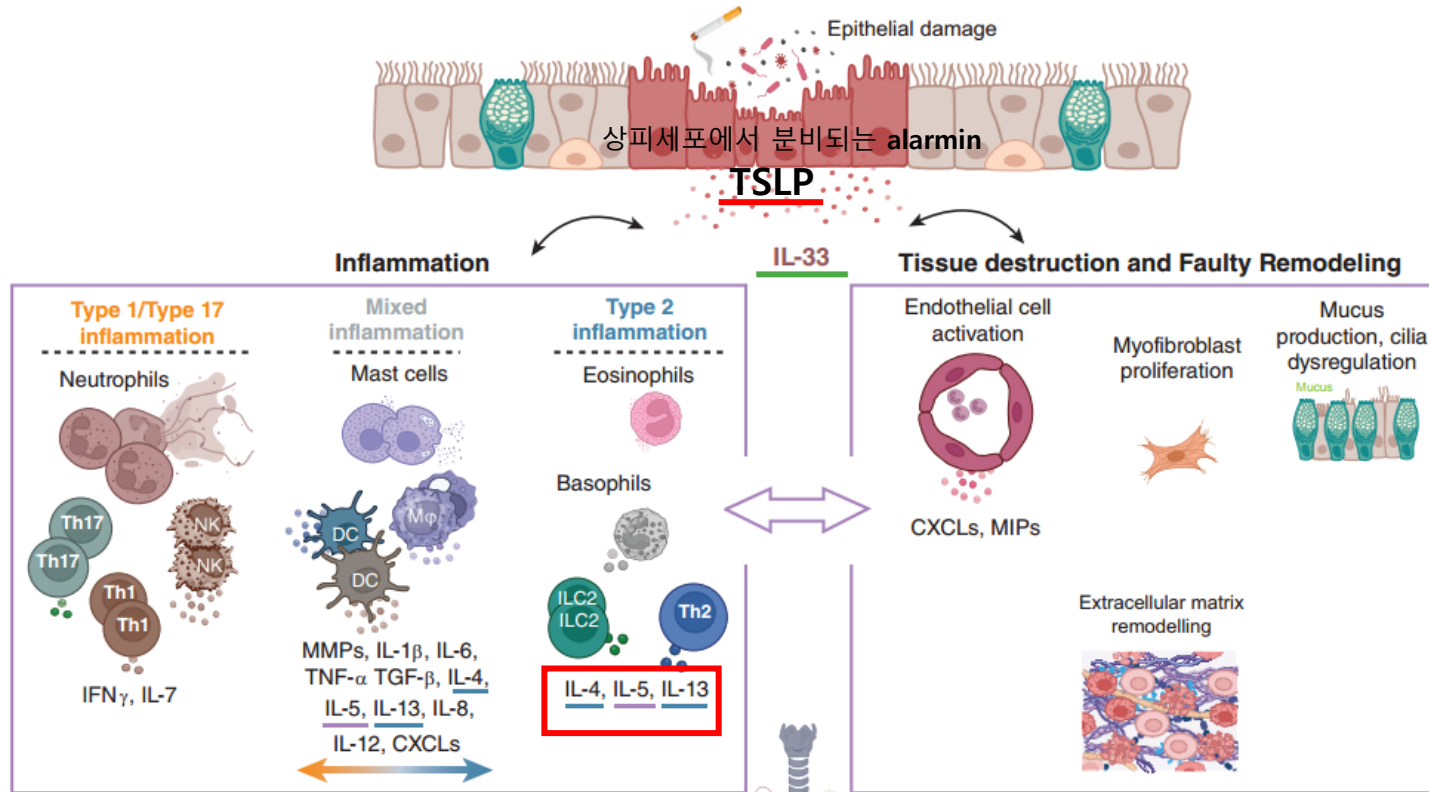


Table 3. Post hoc analysis for risk of AECOPD based on COVID-19 status

Population	COVID-19	Number	Number of AECOPD	AECOPD, /10,000 population	HR (95% CI)	Adjusted HR (95% CI)
Vaccinated	No	1,731	70	1,679	Reference	Reference
	Yes	70	3	1,781	1.06 (0.33–3.36)	1.35 (0.42–4.36)
Unvaccinated	No	1,655	124	3,190	Reference	Reference
	Yes	146	20	5,966	1.86 (1.16–2.98)	2.06 (1.28–3.33)



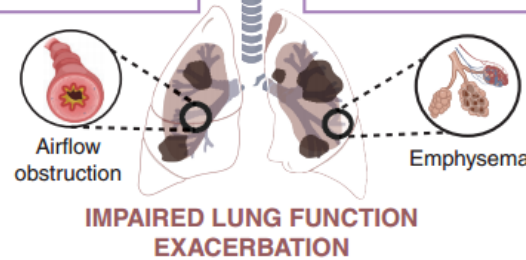
# ExCOPD의 예방/치료 - (2-1) EO inflammation



IL 4/13 Rc : Dupilumab

IL-5 : Mepolizumab

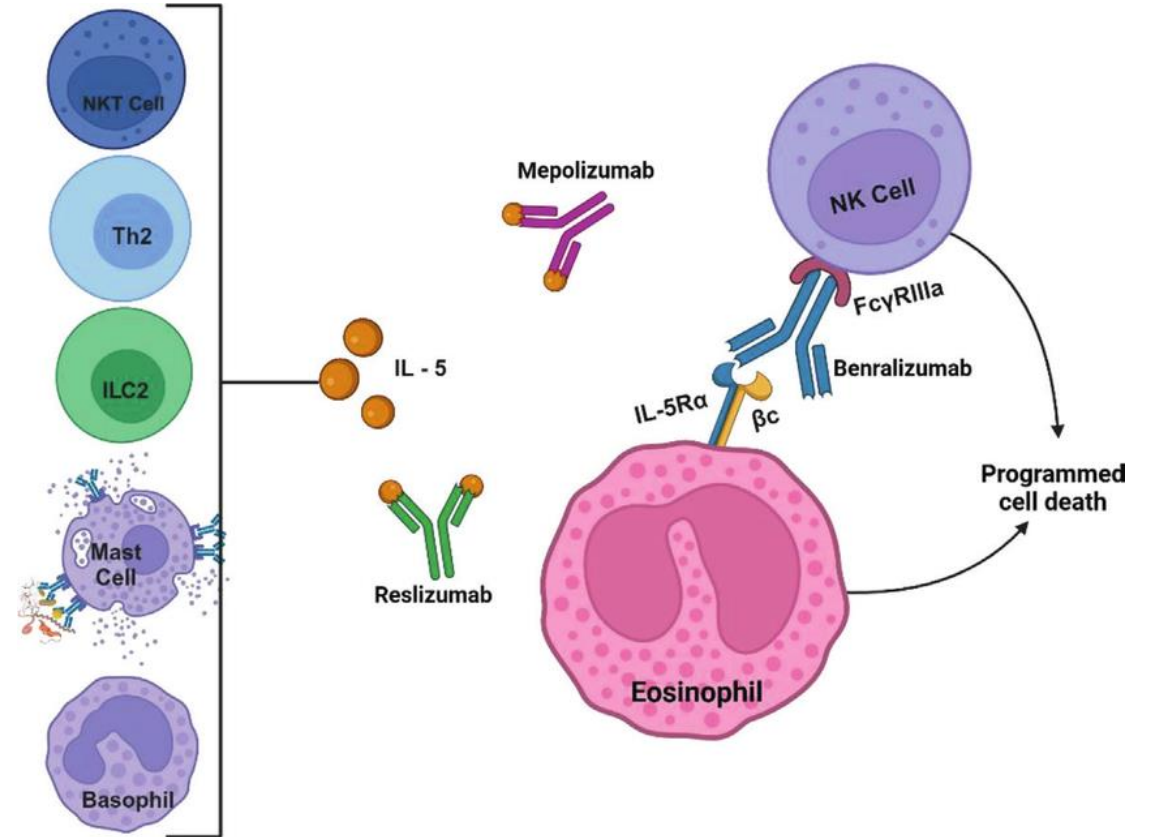
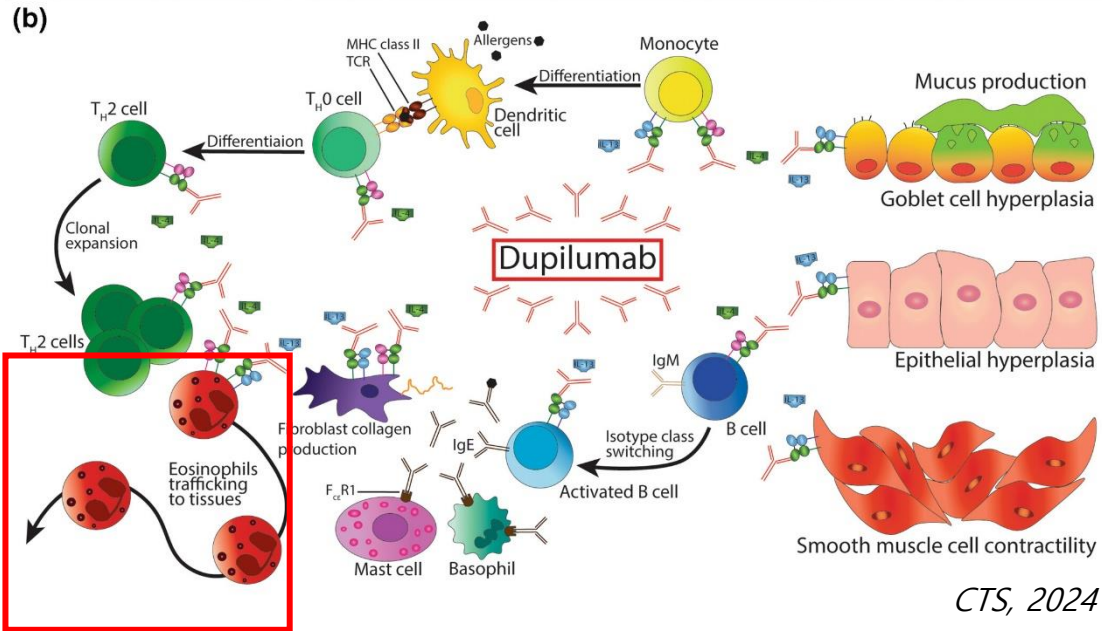
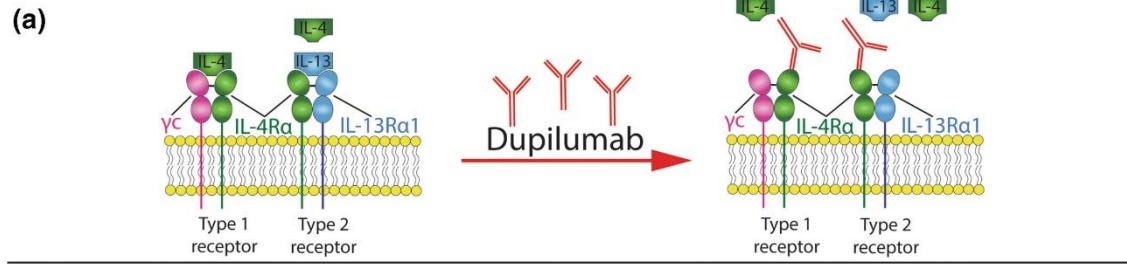
IL-5 Rc : Benralizumab



Targeted by: — Itepekimab, tozurakimab — Dupilumab — Mepolizumab, benralizumab — Tezepelumab



# ExCOPD의 예방/치료 - (2-1) EO inflammation



*Eosinophils and Their Role in Human Health and Disease, 2024*

IL 4/13 Rc : Dupilumab → **IL-4/IL-13 pathway 전체 억제**, 넓은 범위의 Type 2 염증 억제

IL-5 : Mepolizumab → IL-5를 중화해 호산구 생존 신호 차단

IL-5 Rc : Benralizumab → IL-5Rc에 붙어 NK세포로 하여금 호산구를 직접 죽이게 함 (ADCC)



# ExCOPD의 예방/치료 - (2-1) EO inflammation

## Dupilumab for chronic obstructive pulmonary disease with type 2 inflammation: a pooled analysis of two phase 3, randomised, double-blind, placebo-controlled trials

Surya P Bhatt\*, Klaus F Rabe\*, Nicola A Hanania, Claus F Vogelmeier, Mona Bafadhel, Stephanie A Christenson, Alberto Papi, Dave Singh, Elizabeth Laws, Paula Dakin, Jennifer Maloney, Xin Lu, Deborah Bauer, Ashish Bansal, Raolat M Abdulai, Lacey B Robinson

항목	BOREAS Trial	NOTUS Trial
연도	2023 (NEJM)	2024 (NEJM/Press release)
연구 디자인	Phase 3, RCT, 무작위, 이중맹검, 위약 대조	
약제	<b>Dupilumab 300 mg SC Q2W</b>	
배경 치료	ICS/LABA/LAMA triple inhaler 유지	
대상 지역	미국·유럽·아시아 포함	다국가
주요 목적	COPD 악화 감소 및 폐기능 개선 확인	
Inclusion criteria	<b>연령</b> : 40-85 yrs <b>COPD 진단</b> : GOLD 기준 <b>흡입기 치료</b> : ICS + LABA + LAMA ≥3개월, except ICS for contraindication <b>혈중 호산구</b> : ≥300 cells/ $\mu$ L <b>악화력</b> : 지난 1년간 moderate ≥2회 or severe COPDEx ≥1회 <b>흡연력</b> : ≥10 pack-years <b>FEV1</b> : 30-70% predicted	

Dupilumab group  
938 (50.1%)  
SC 300mg every 2weeks  
for 52weeks

1:1  
matched

Placebo group  
936 (49.9%)

	Placebo (n=936)	Dupilumab (n=938)	Overall (n=1874)
Age, years	65.0 (8.3)	65.1 (8.0)	65.1 (8.2)
Sex			
Female	302 (32.3%)	320 (34.1%)	622 (33.2%)
Male	634 (67.7%)	618 (65.9%)	1252 (66.8%)
Region*			
Asia	66 (7.1%)	67 (7.1%)	133 (7.1%)
Latin America	256 (27.4%)	255 (27.2%)	511 (27.3%)
Eastern Europe	358 (38.2%)	361 (38.5%)	719 (38.4%)
High-income	256 (27.4%)	255 (27.2%)	511 (27.3%)
Race			
White	813 (86.9%)	815 (86.9%)	1628 (86.9%)
Black	10 (1.1%)	7 (0.7%)	17 (0.9%)
Asian	70 (7.5%)	74 (7.9%)	144 (7.7%)
American Indian or Alaskan Native	30 (3.2%)	25 (2.7%)	55 (2.9%)
Native Hawaiian or Pacific Islander	1 (0.1%)	1 (0.1%)	2 (0.1%)
Multiple	12 (1.3%)	16 (1.7%)	28 (1.5%)
Ethnicity			
Hispanic or Latino	278 (29.7%)	283 (30.2%)	561 (29.9%)
Non-Hispanic or non-Latino	650 (69.4%)	650 (69.3%)	1300 (69.4%)
Unknown	8 (0.9%)	5 (0.5%)	13 (0.7%)
Smoking status			
Former	654 (69.9%)	662 (70.6%)	1316 (70.2%)
Current	282 (30.1%)	276 (29.4%)	558 (29.8%)
Smoking history, pack-years	38 (22-50)	35 (22-48)	36 (22-50)
Emphysema	301 (32.2%)	289 (30.8%)	590 (31.5%)
BMI, kg/m <sup>2</sup>	27.7 (5.6)	27.8 (5.4)	27.8 (5.5)
Triple therapy (ie, inhaled corticosteroid, long-acting $\beta$ 2-agonist, and long-acting muscarinic antagonist)	919 (98.2%)	921 (98.2%)	1840 (98.2%)
Moderate or severe COPD exacerbations in the previous year	2.2 (0.9)	2.2 (1.0)	2.2 (1.0)
≥1 severe COPD exacerbation in the previous year	214 (22.9%)	242 (25.8%)	456 (24.3%)

	Placebo (n=936)	Dupilumab (n=938)	Overall (n=1874)
(Continued from previous column)			
Lung function			
Pre-bronchodilator FEV <sub>1</sub> , L	1.4 (0.5)	1.3 (0.5)	1.3 (0.5)
Post-bronchodilator FEV <sub>1</sub> , L	1.4 (0.5)	1.4 (0.5)	1.4 (0.5)
Post-bronchodilator FEV <sub>1</sub> , predicted value	50.7% (12.8)	50.0% (13.0)	50.3% (12.9)
Post-bronchodilator FEV <sub>1</sub> /FVC ratio	0.49 (0.12)	0.49 (0.12)	0.49 (0.12)
St George's Respiratory Questionnaire total score	49.8 (17.2)	50.2 (17.4)	50.0 (17.3)
Evaluating Respiratory Symptoms in COPD total score	13.1 (8.3-17.9)	12.7 (8.4-17.7)	13.0 (8.3-17.8)
Biomarkers of type 2 inflammation			
Baseline blood eosinophil count, cells per $\mu$ L	330 (230-460)	340 (240-460)	330 (230-460)
Blood eosinophil category at randomisation			
<300 cells/ $\mu$ L	374 (40.0%)	364 (38.8%)	738 (39.4%)
≥300 cells/ $\mu$ L	562 (60.0%)	573 (61.1%)	1135 (60.6%)
Fractional exhaled nitric oxide	17 (10-30)	17 (10-29)	17 (10-30)
<20 ppb	494/865 (57.1%)	495/862 (57.4%)	989/1727 (57.3%)
≥20 ppb	371/865 (42.9%)	367/862 (42.6%)	738/1727 (42.7%)
Data are n (%), n/N (%), mean (SD), or median (IQR). COPD=chronic obstructive pulmonary disease. FVC=forced vital capacity. ppb=parts per billion. *Asia refers to Japan, China, and South Korea. Latin America refers to Argentina, Colombia, Peru, Chile, Brazil, and Mexico. Eastern Europe refers to Russia, Ukraine, Poland, Bulgaria, Lithuania, Latvia, the Czech Republic, Slovakia, Romania, Serbia, Türkiye, and Hungary. High-income refers to Australia, Belgium, France, Portugal, Spain, Germany, the Netherlands, the UK, South Africa, Canada, the USA, Greece, Finland, Denmark, Israel, Sweden, and Italy.			
Table 1: Pooled baseline demographics and disease characteristics			

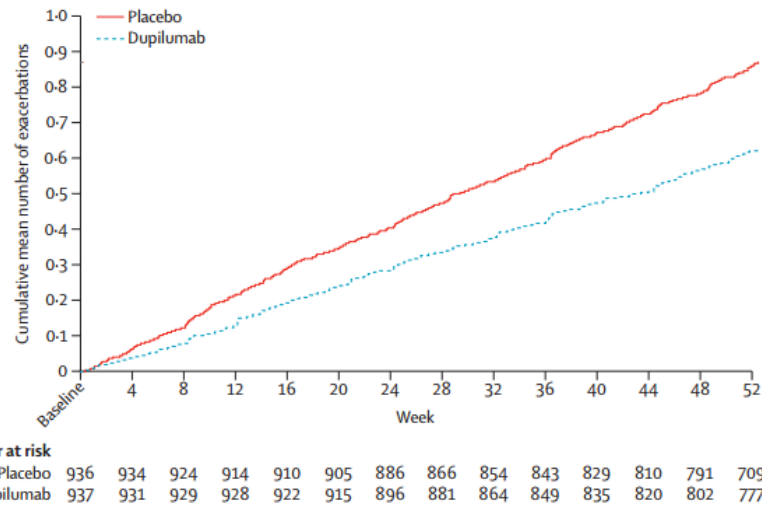


# ExCOPD의 예방/치료 - (2-1) EO inflammation

	Placebo (n=936)*	Dupilumab (n=938)*	Difference vs placebo (95% CI)†	Nominal p value‡
<b>Primary outcome</b>				
Annualised rate of moderate or severe COPD exacerbation during the 52-week treatment period§	1-156	0-794	0-687 (0-595 to 0-793)	<0-0001
<b>Secondary or other outcomes</b>				
Change in pre-bronchodilator FEV <sub>1</sub> from baseline to week 12 compared with placebo, L	0-064 (0-013)	0-147 (0-013)	0-083 (0-053 to 0-112)	<0-0001
Change in pre-bronchodilator FEV <sub>1</sub> from baseline to week 52 compared with placebo, L	0-059 (0-015)	0-133 (0-015)	0-073 (0-040 to 0-107)	<0-0001
Change in pre-bronchodilator FEV <sub>1</sub> from baseline to week 12 compared with placebo in patients with baseline FeNO ≥20 ppb¶, L	0-089 (0-027)	0-219 (0-027)	0-131 (0-074 to 0-187)	<0-0001
Change in pre-bronchodilator FEV <sub>1</sub> from baseline to week 52 compared with placebo in patients with baseline FeNO ≥20 ppb¶, L	0-104 (0-029)	0-210 (0-029)	0-106 (0-042 to 0-170)	0-0012
Change from baseline to week 52 in SGRQ total score compared with placebo	-6-579 (0-640)	-9-945 (0-636)	-3-366 (-4-953 to -1-778)	<0-0001
Proportion of patients with SGRQ improvement ≥4 points at week 52 compared with placebo	370/830 (44-6%)	427/830 (51-5%)	1-311 (1-070 to 1-607)	0-0089
Change in Evaluating Respiratory Symptoms in COPD total score from baseline to week 52 compared with placebo	-1-605 (0-200)	-2-519 (0-201)	-0-914 (-1-438 to -0-389)	0-0006
Annualised rate of moderate or severe COPD exacerbation compared with placebo during the 52-week treatment period in patients with baseline FeNO ≥20 ppb¶	1-321	0-729	0-552 (0-434 to 0-701)	<0-0001
Annualised rate of severe COPD exacerbation compared with placebo during the 52-week treatment period	0-124	0-084	0-674 (0-438 to 1-037)	0-073

Reduction in the annualized rate of moderate to severe exacerbation

A



	Placebo (n)	Dupilumab (n)	Incidence rate ratio (95% CI)	P-interaction
Age group				
<65 years	414	388	0-651 (0-525-0-808)	0-50
≥65 years	522	550	0-716 (0-590-0-870)	
Age group				
40-64 years	414	388	0-651 (0-525-0-808)	0-70
65-74 years	394	434	0-741 (0-594-0-925)	
75-85 years	128	116	0-681 (0-453-1-022)	
Sex				
Male	634	618	0-687 (0-575-0-821)	0-96
Female	302	320	0-690 (0-538-0-883)	
Smoking status at screening				
Current	282	276	0-683 (0-528-0-884)	0-85
Former	654	662	0-685 (0-576-0-815)	
Number of moderate or severe COPD exacerbations in previous year before visit 1				
≤2	751	752	0-713 (0-599-0-849)	0-63
3	140	114	0-565 (0-401-0-795)	
≥4	45	72	0-616 (0-417-0-911)	
Number of severe COPD exacerbations in previous year before visit 1				
0	722	695	0-686 (0-579-0-812)	0-94
1	181	198	0-720 (0-532-0-976)	
≥2	33	44	0-585 (0-313-1-094)	
Number of severe COPD exacerbations in previous year before visit 1				
0	722	695	0-686 (0-579-0-812)	0-96
≥1	214	242	0-684 (0-520-0-901)	
Baseline predicted post-bronchodilator FEV <sub>1</sub>				
<50%	468	477	0-705 (0-584-0-852)	0-64
≥50%	467	458	0-658 (0-526-0-823)	
Comorbid ongoing history of emphysema				
Yes	301	289	0-658 (0-526-0-823)	0-66
No	635	649	0-703 (0-584-0-848)	
Baseline BODE score				
≤4	602	561	0-678 (0-558-0-824)	0-87
>4	339	367	0-673 (0-542-0-833)	
Baseline fractional exhaled nitric oxide				
<20 ppb	494	495	0-824 (0-680-1-000)	0-010
≥20 ppb	371	367	0-552 (0-434-0-701)	
Baseline serum total IgE				
<100 IU/mL	416	390	0-761 (0-613-0-943)	0-29
≥100 IU/mL	469	507	0-632 (0-517-0-773)	
Baseline eosinophil count				
<300 cells per µL	374	364	0-655 (0-517-0-829)	0-76
≥300 cells per µL	562	573	0-700 (0-583-0-840)	
Race				
Black*	14	12	0-491 (0-113-2-125)	NA
Not Black	922	926	0-689 (0-596-0-796)	

High FENO → good effect for dupilumab

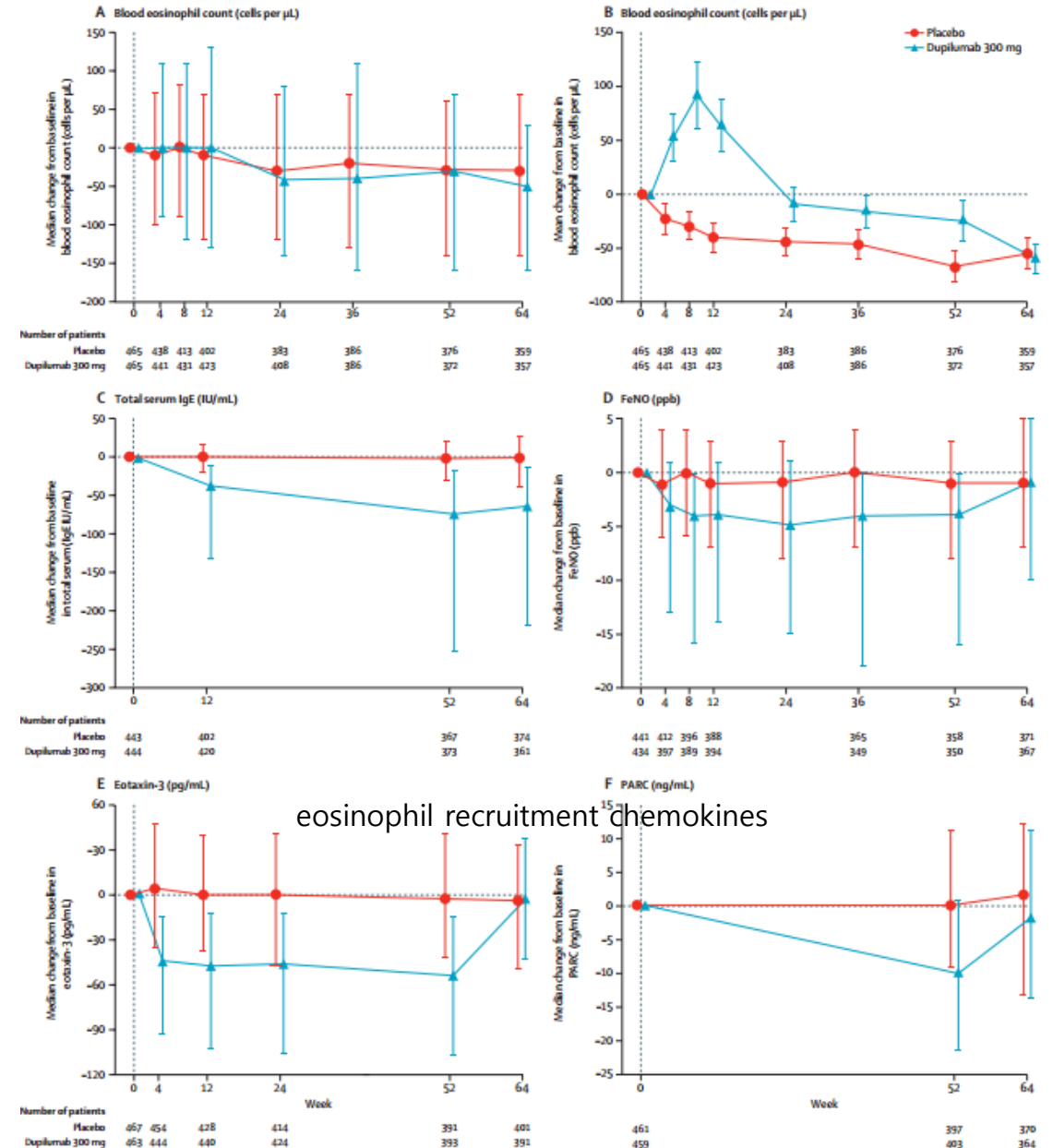


# ExCOPD의 예방/치료 – (2-1) EO inflammation

Type 2 inflammation biomarkers and their association with response to dupilumab in COPD (BOREAS): an analysis of a randomised, placebo-controlled, phase 3 trial

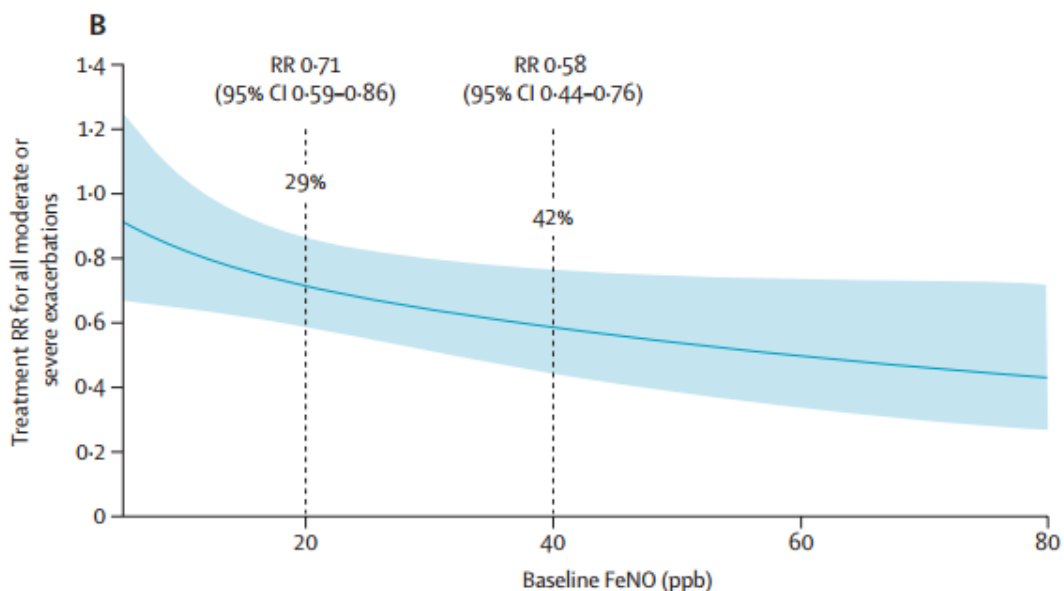
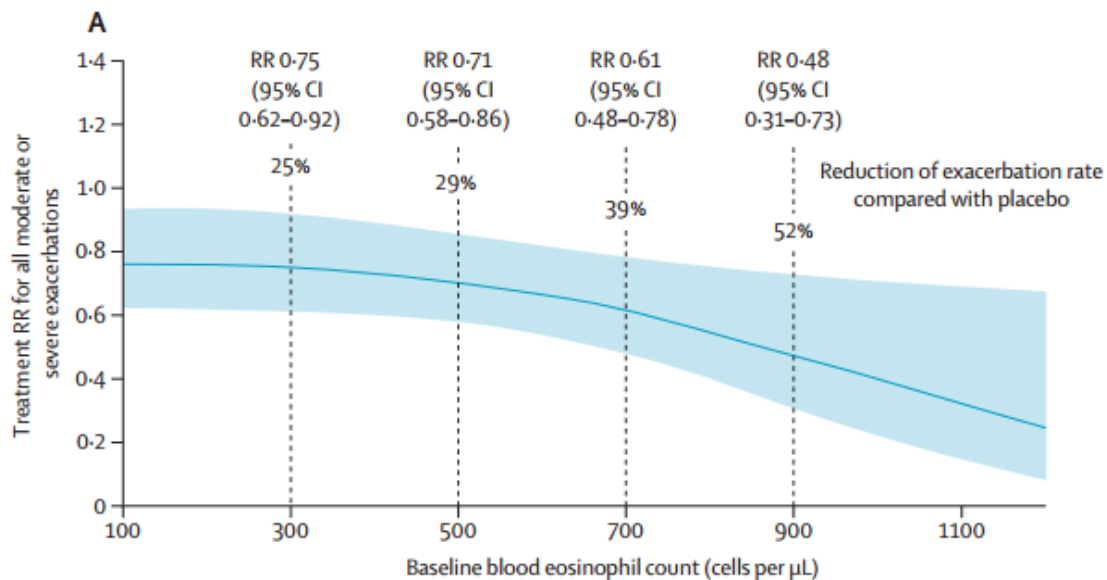
Stephanie A Christenson, Nicola A Hanania, Surya P Bhatt, Mona Bafadhel, Klaus F Rabe, Claus F Vogelmeier, Alberto Papi, Dave Singh, Elizabeth Laws, Paula Dakin, Ashish Bansal, Xin Lu, Deborah Bauer, Jennifer Maloney, Lacey B Robinson, Raolat M Abdulul

	Placebo group (n=471)	Dupilumab group (n=468)
Age, years	65.2 (8.1)	65.0 (8.0)
Sex		
Female	149 (32%)	170 (36%)
Male	322 (68%)	298 (64%)
Race or ethnicity		
White	397 (84%)	393 (84%)
Black or of African descent	2 (<1%)	3 (1%)
Asian	67 (14%)	67 (14%)
American Indian or Alaska Native	4 (1%)	3 (1%)
Native Hawaiian or Pacific Islander	1 (<1%)	0
Multiple	0	2 (<1%)
BMI, kg/m <sup>2</sup>	27.7 (5.7)	27.5 (5.4)
Smoking status		
Former	323 (69%)	334 (71%)
Current	148 (31%)	134 (29%)
Smoking history, pack-years	39.0 (22.5–50.0)	35.0 (23.0–48.0)
High-dose inhaled corticosteroid from medication history	126 (27%)	131 (28%)
Moderate or severe exacerbations in the previous year	2.3 (1.0)	2.2 (1.1)
Pre-bronchodilator FEV <sub>1</sub> , L	1.3 (0.5)	1.3 (0.5)
Post-bronchodilator FEV <sub>1</sub> , L	1.4 (0.5)	1.4 (0.5)
Blood eosinophil count, cells per $\mu$ L		
At screening	430.0 (340.0–600.0)	420.0 (350.0–540.0)
At baseline	330.0 (230.0–460.0)	340.0 (250.0–460.0)
<300 cells/ $\mu$ L at baseline	186 (39%)	180 (38%)
$\geq$ 300 cells/ $\mu$ L at baseline	285 (61%)	288 (62%)
Total serum IgE, IU/mL	120.5 (41.1–407.0)	120.5 (45.1–415.0)
FeNO, ppb	17.0 (11.0–30.0)	17.0 (10.0–31.0)
FeNO group		
<20 ppb	254/442 (57%)	238/433 (55%)
$\geq$ 20 ppb	188/422 (45%)	195/433 (45%)
Plasma eotaxin-3, pg/mL	154.0 (109.0–221.5)	146.0 (105.0–219.0)
Serum PARC, ng/mL	72.1 (54.0–94.9)	72.3 (54.9–97.8)





# ExCOPD의 예방/치료 - (2-1) EO inflammation



## DUPILUMAB

### TYPE 2 INFLAMMATION

EOSINOPHIL  
REDUCTION



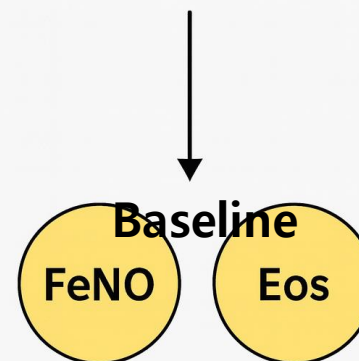
Not  
APPROPRIATE  
MARKER

FeNO



APPROPRIATE  
MARKER

Biomarkers predicting  
reduced moderate or  
severe exacerbations  
with Dupilumab





# ExCOPD의 예방/치료 – (2-1) EO inflammation

The NEW ENGLAND JOURNAL of MEDICINE

## Mepolizumab to Prevent Exacerbations of COPD with an Eosinophilic Phenotype

F.C. Scirba,<sup>1</sup> G.J. Criner,<sup>2</sup> S.A. Christenson,<sup>3</sup> F.J. Martinez,<sup>4</sup> A. Papi,<sup>5</sup> N. Roche,<sup>6</sup> J. Bourbeau,<sup>7</sup> S. Korn,<sup>8</sup> M. Bafadhel,<sup>9</sup> M.L.K. Han,<sup>10</sup> S. Kolterer,<sup>11</sup> K. Miller,<sup>12</sup> D. Mouneimne,<sup>13</sup> J. Fletcher,<sup>13</sup> B. Mayer,<sup>14</sup> J. Min,<sup>15</sup> and I.D. Pavord,<sup>16</sup> for the MATINEE Study Investigators\*

- Methods
  - MATINEE : a phase 3, double-blind, randomized, placebo-controlled trial conducted at 344 centers in 25 countries
  - October 2019 through August 2023
- Inclusion criteria
  - Patients with COPD
  - History of exacerbation (지난 1년간 moderate ≥2회 or severe COPDex ≥1회 )
  - **Blood eosinophil ≥ 300 cells/uL**
  - **Patients receiving triple inhaled therapy for COPD**

mepolizumab  
(at a dose of 100 mg)  
SC every 4 weeks  
for 58-104 weeks

1:1

Placebo group

**Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.\***

Characteristic	Mepolizumab (N=403)	Placebo (N=401)	Overall (N=804)
Age — yr	66.4±8.1	66.0±7.9	66.2±8.0
Female sex — no. (%)	127 (32)	126 (31)	253 (31)
Smoking status — no. (%)			
Current smoker	111 (28)	111 (28)	222 (28)
Former smoker	292 (72)	290 (72)	582 (72)
Severity of airflow obstruction — no. (%)†			
Mild	2 (<1)	3 (1)	5 (1)
Moderate	168 (42)	181 (45)	349 (43)
Severe	180 (45)	160 (40)	340 (42)
Very severe	53 (13)	57 (14)	110 (14)
Moderate or severe exacerbations ≤12 mo before screening			
No. per patient	2.3±1.0	2.2±0.9	2.3±0.9
≥1 moderate exacerbation — no. (%)	350 (87)	348 (87)	698 (87)
≥1 severe exacerbation — no. (%)	88 (22)	77 (19)	165 (21)
Geometric mean blood eosinophil count ±log SD — cells/μl	480±0.378	480±0.398	480±0.388
Coexisting condition — no. (%)‡			
Previous or current diagnosis of cardiac disease	103 (26)	97 (24)	200 (25)
Previous or current risk factor for cardiovascular disease	289 (72)	288 (72)	577 (72)
Previous diagnosis of pneumonia	75 (19)	63 (16)	138 (17)
mMRC dyspnea scale grade at screening — no. (%)§			
<2	89 (22)	98 (24)	187 (23)
≥2	310 (77)	301 (75)	611 (76)
Missing data	4 (1)	2 (<1)	6 (1)
Health-related quality of life¶			
CAT score	19.2±7.0	19.1±6.8	19.2±6.9
SGRQ total score	55.3±17.7	53.9±17.9	54.6±17.8
E-RS-COPD total score	13.2±6.8	12.9±6.8	13.1±6.8
Symptoms of chronic bronchitis — no. (%)			
Present	277 (69)	267 (67)	544 (68)
Absent	113 (28)	126 (31)	239 (30)
Unknown	13 (3)	8 (2)	21 (3)

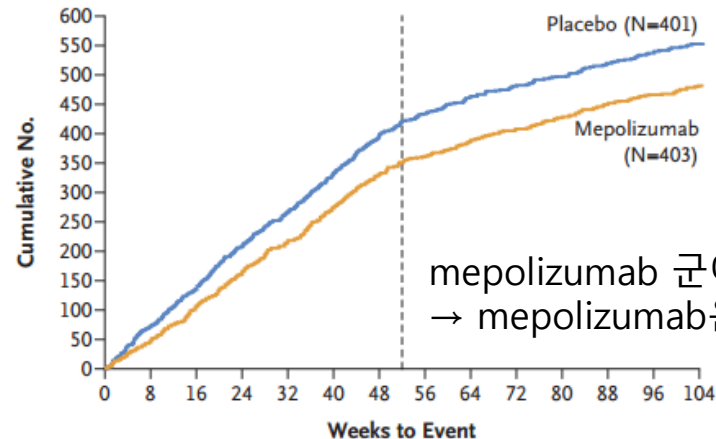


# ExCOPD의 예방/치료 – (2-1) EO inflammation

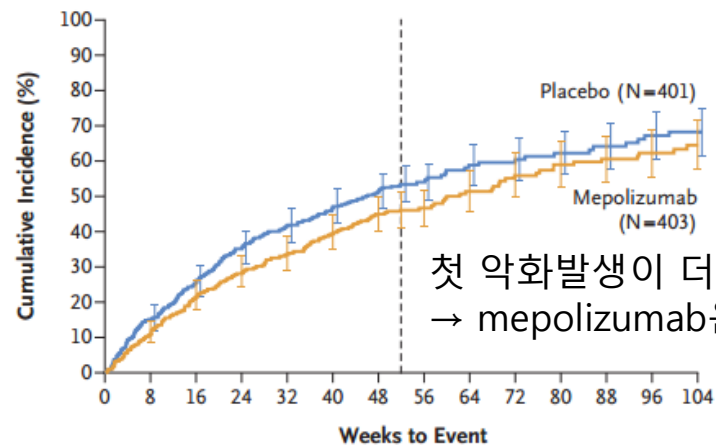
Table 2. Primary and Secondary Efficacy End Points.\*

End Point	Mepolizumab (N=403)	Placebo (N=401)
<b>Primary end point</b>		
Annualized rate of moderate or severe exacerbations (95% CI) — events/yr	0.80 (0.70–0.91)	1.01 (0.89–1.15)
Rate ratio vs. placebo (95% CI)	0.79 (0.66–0.94)	—
P value	0.01	—
<b>Secondary end points</b>		
Time to first moderate or severe exacerbation		
Kaplan–Meier median time to first moderate or severe exacerbation (95% CI) — days	419 (332–530)	321 (262–396)
Estimated risk of a moderate or severe exacerbation up to wk 104 (95% CI) — %	64.5 (57.5–71.4)	68.3 (61.4–74.9)
Hazard ratio for the first moderate or severe exacerbation up to wk 104 vs. placebo (95% CI)	0.77 (0.64–0.93)	—
P value	0.009	—
Response, defined as a decrease in the CAT score†‡		
No. of patients with a response (%)	162 (41)	180 (46)
No. of patients without a response (%)	220 (56)	206 (52)
Odds ratio of response vs. placebo (95% CI)	0.81 (0.60–1.09)	—
Relative risk of response vs. placebo (95% CI)§	0.92 (0.81–1.05)	—
Response, defined as a decrease in the SGRQ total score¶		
No. of patients with a response (%)	195 (50)	179 (46)
No. of patients without a response (%)	186 (48)	206 (52)
Odds ratio of response vs. placebo (95% CI)	1.17 (0.87–1.57)	—
Relative risk of response vs. placebo (95% CI)§	1.04 (0.91–1.20)	—
Response, defined as a decrease in the E-RS–COPD total score		
No. of patients with a response (%)	123 (31)	137 (34)
No. of patients without a response (%)	271 (67)	254 (64)
Odds ratio of response vs. placebo (95% CI)	0.82 (0.60–1.12)	—
Relative risk of response vs. placebo (95% CI)§	0.87 (0.72–1.04)	—
Annualized rate of exacerbations resulting in emergency department visit, hospitalization, or both		
Events/yr (95% CI)	0.13 (0.10–0.18)	0.20 (0.15–0.27)
Rate ratio vs. placebo (95% CI)	0.65 (0.43–0.96)	—

A Moderate or Severe Exacerbations



B First Moderate or Severe Exacerbation



No. at Risk

	0	8	16	24	32	40	48	56	64	72	80	88	96	104
Placebo	401	333	292	250	223	203	180	71	56	46	41	37	32	22
Mepolizumab	403	355	309	277	251	222	202	82	69	58	52	48	41	24



# ExCOPD의 예방/치료 – (2-1) EO inflammation

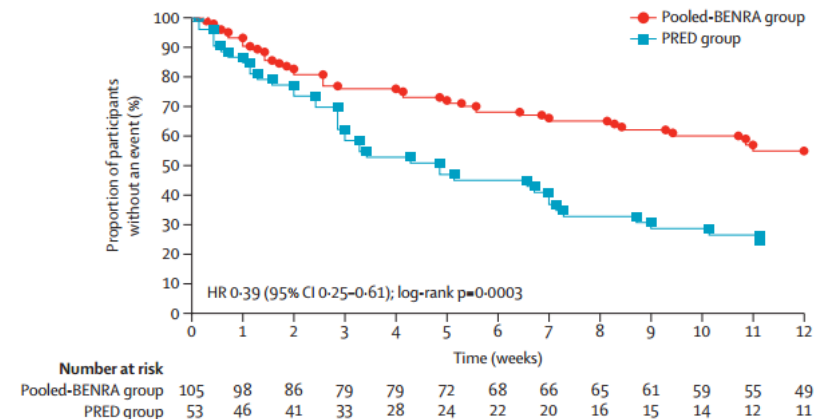
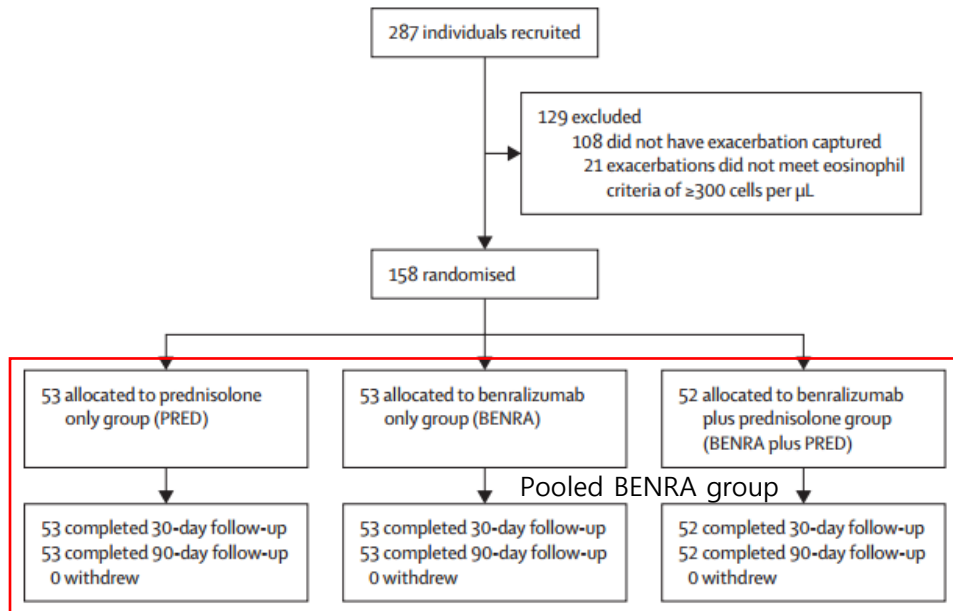
Treating eosinophilic exacerbations of asthma and COPD with benralizumab (ABRA): a double-blind, double-dummy, active placebo-controlled randomised trial

*Sanjay Ramakrishnan, Richard E K Russell, Hafiz R Mahmood, Karolina Krassowska, James Melhorn, Christine Mwasuku, Ian D Pavord, Laura Bermejo-Sanchez, Imran Howell, Mahdi Mahdi, Stefan Peterson, Thomas Bengtsson, Mona Bafadhel*

- Method
- ABRA Trial : multicentre, phase 2, double-blind, double-dummy, active placebo-controlled randomised trial completed in the UK
- **At the time of an AE of asthma or COPD, adults with blood eosinophil counts of  $\geq 300$  cells per  $\mu\text{L}$**
- randomly assigned in a 1:1:1 ratio (prednisolone 30 mg for 5 days, 100 mg benralizumab SC, dual)

\* Treatment failure  
Death  
Admission to hospital  
Retreatment (steroid or anti)

	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

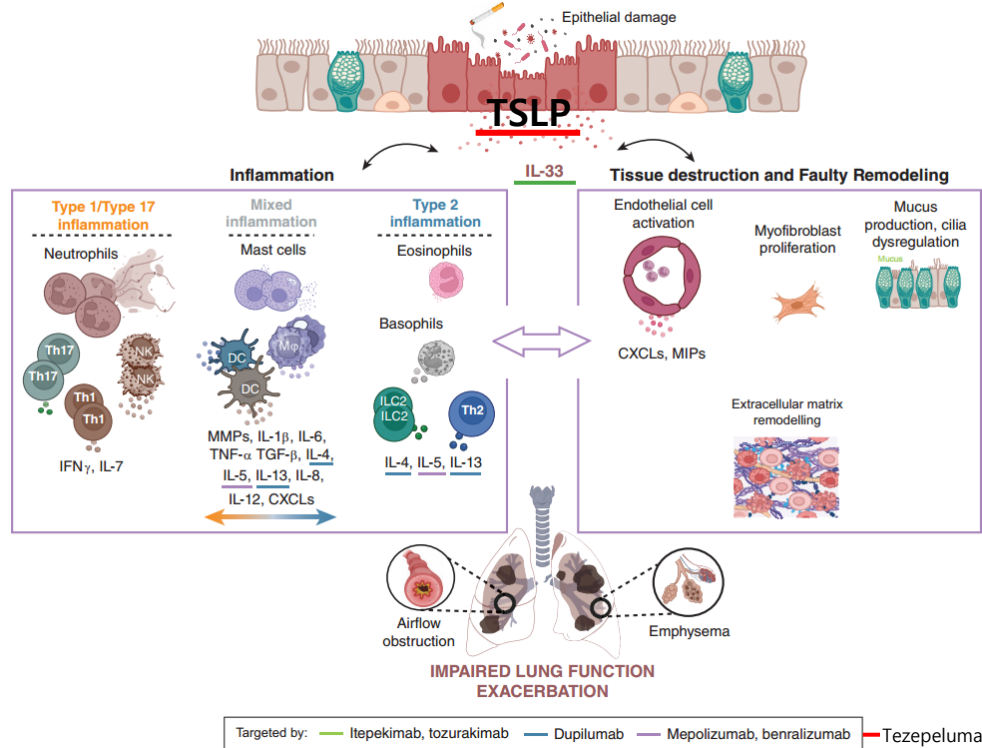


급성 악화 치료로 benralizumab의 사용이 이후 경과를 바꿀 수 있다.



# ExCOPD의 예방/치료 - (2-2) anti-inflammation

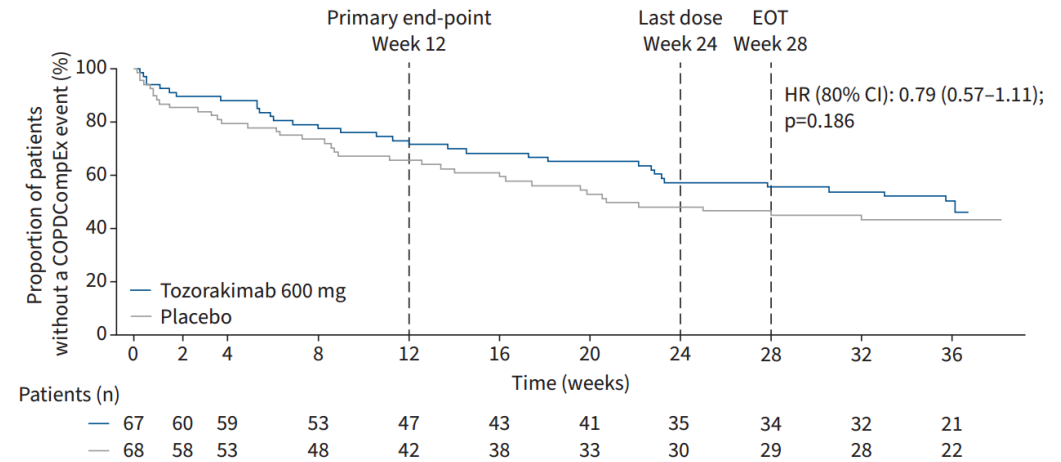
TLSP : Tezepelumab  
IL-33 : Tozorakimab



EUROPEAN RESPIRATORY JOURNAL  
ORIGINAL RESEARCH ARTICLE  
D. SINGH ET AL.

## A phase 2a trial of the IL-33 monoclonal antibody **tozorakimab** in patients with COPD: FRONTIER-4

Dave Singh, Patricia Guller, Fred Reid, Sarah Doffman, Ulla Seppälä, Ioannis Psallidas, Rachel Moate, Rebecca Smith, Joanna Kiraga, Eulalia Jimenez, Dennis Brooks, Aoife Kelly, Lars H. Nordenmark, Muhammad Waqas Sadiq, Luis Mateos Caballero, Chris Kell, Maria G. Belvisi and Hitesh Pandya



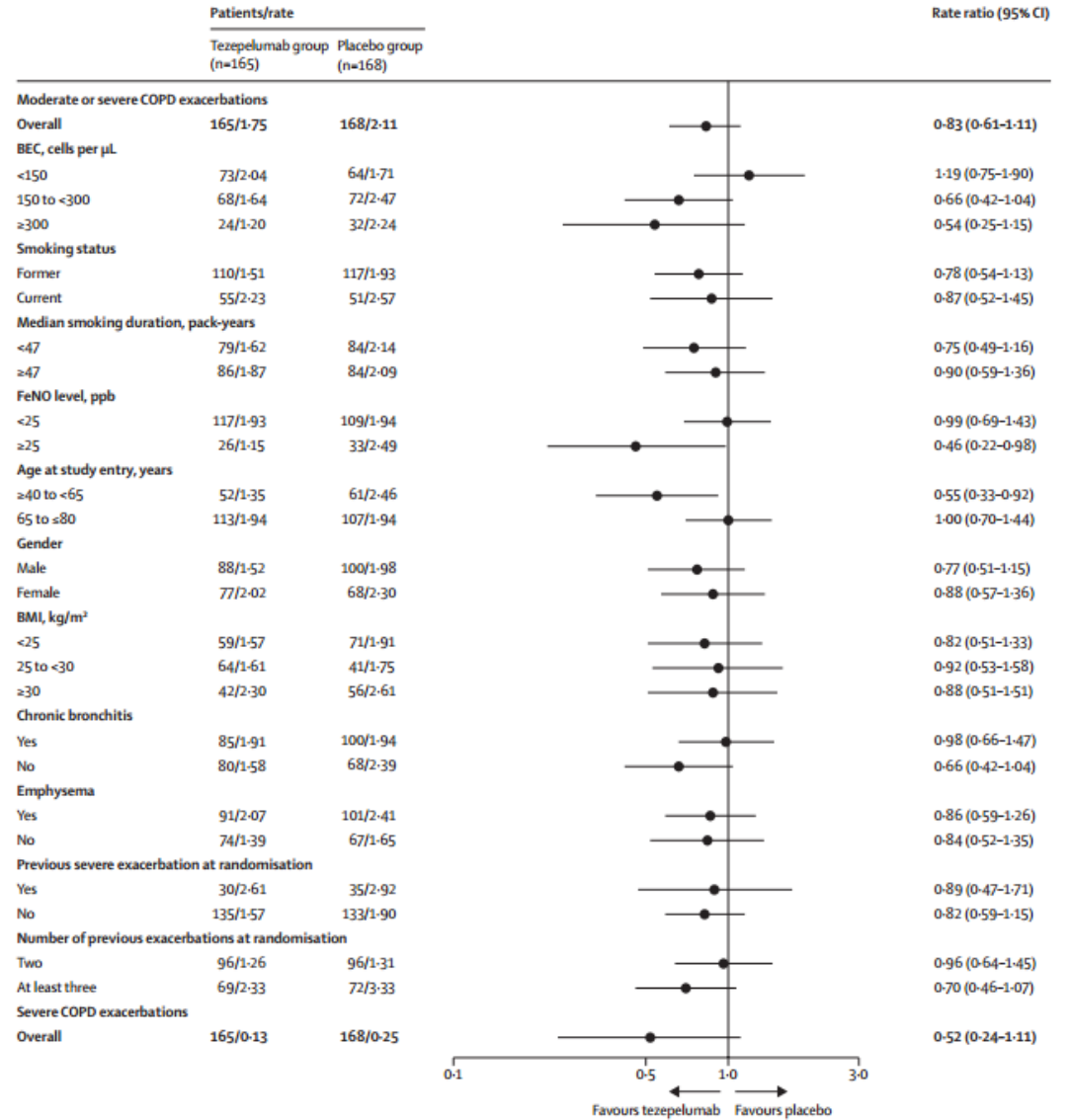
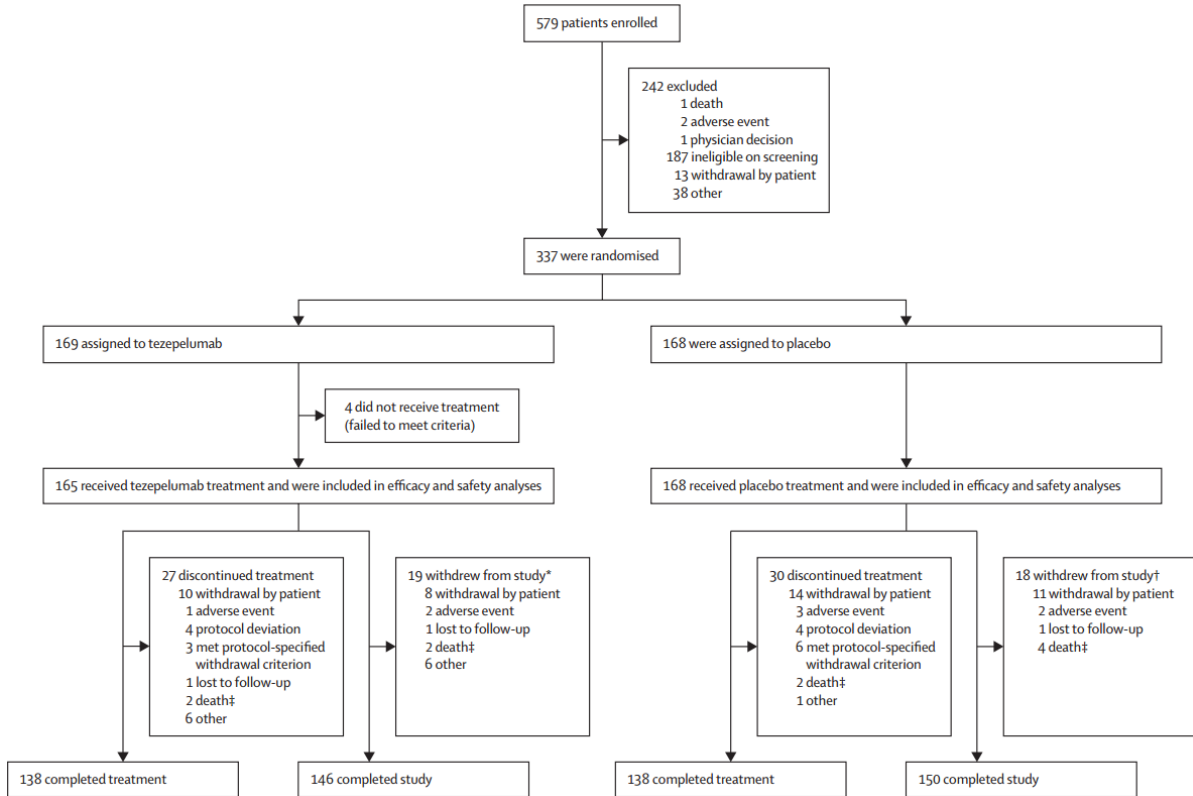
**FIGURE 3** Kaplan-Meier plots of time-to-first COPD composite exacerbation (COPDCompEx) event in the intent-to-treat population. CI: confidence interval; EOT: end of treatment; HR: hazard ratio.



# ExCOPD의 예방/치료 - (2-2) anti-inflammation

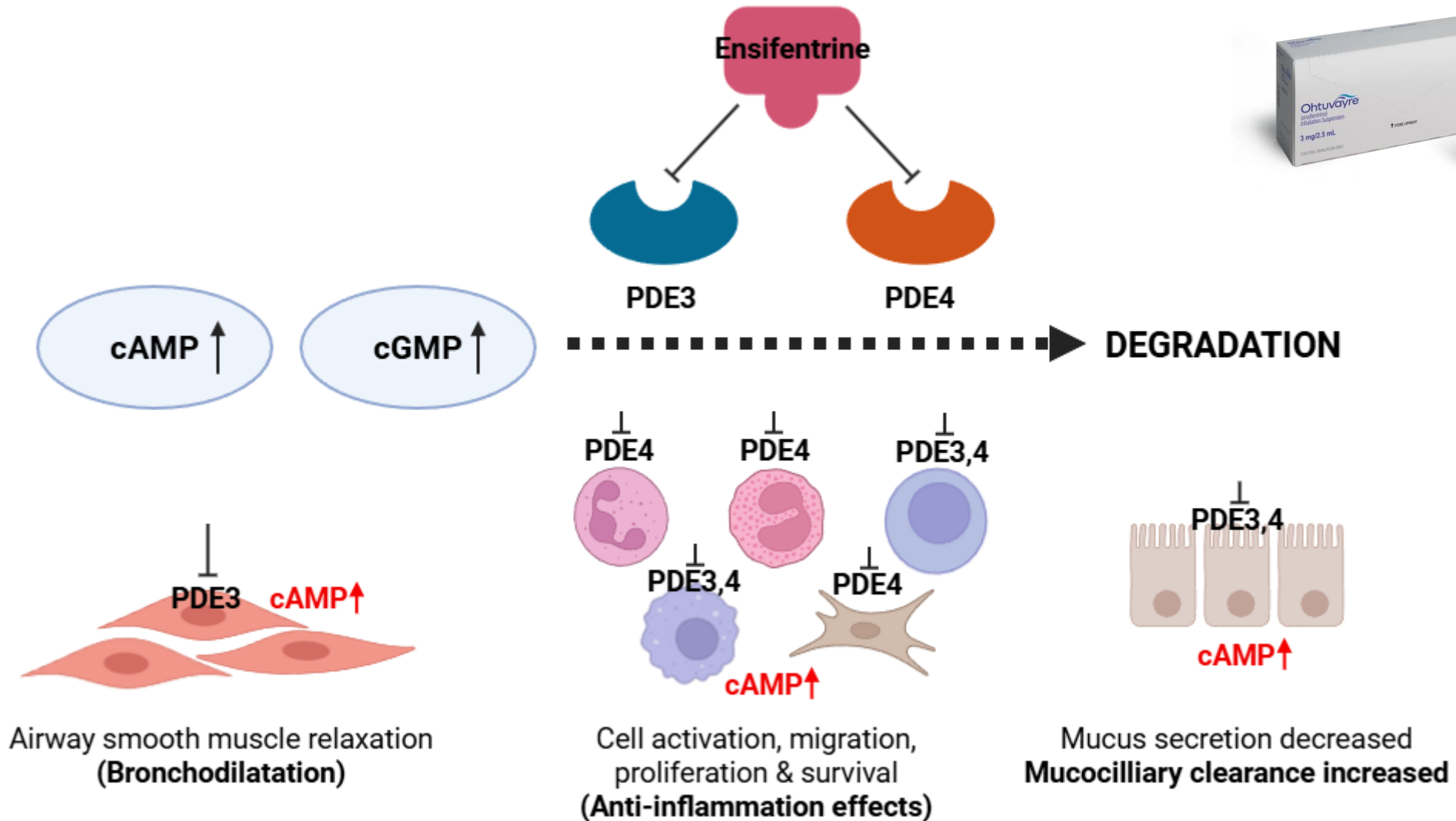
Efficacy and safety of **tezepelumab** versus placebo in adults with moderate to very severe chronic obstructive pulmonary disease (COURSE): a randomised, placebo-controlled, phase 2a trial

*Dave Singh, Christopher E Brightling, Klaus F Rabe, MeiLan K Han, Stephanie A Christenson, M Bradley Drummond, Alberto Papi, Ian D Pavord, Nestor A Molfino, Gun Almqvist, Ales Kotalik, Åsa Hellqvist, Monika Gołqbek, Navreet S Sindhwani, Sandhya S Ponnarambil, on behalf of the COURSE study investigators\**





# ExCOPD의 예방/치료 - (2-2) anti-inflammation



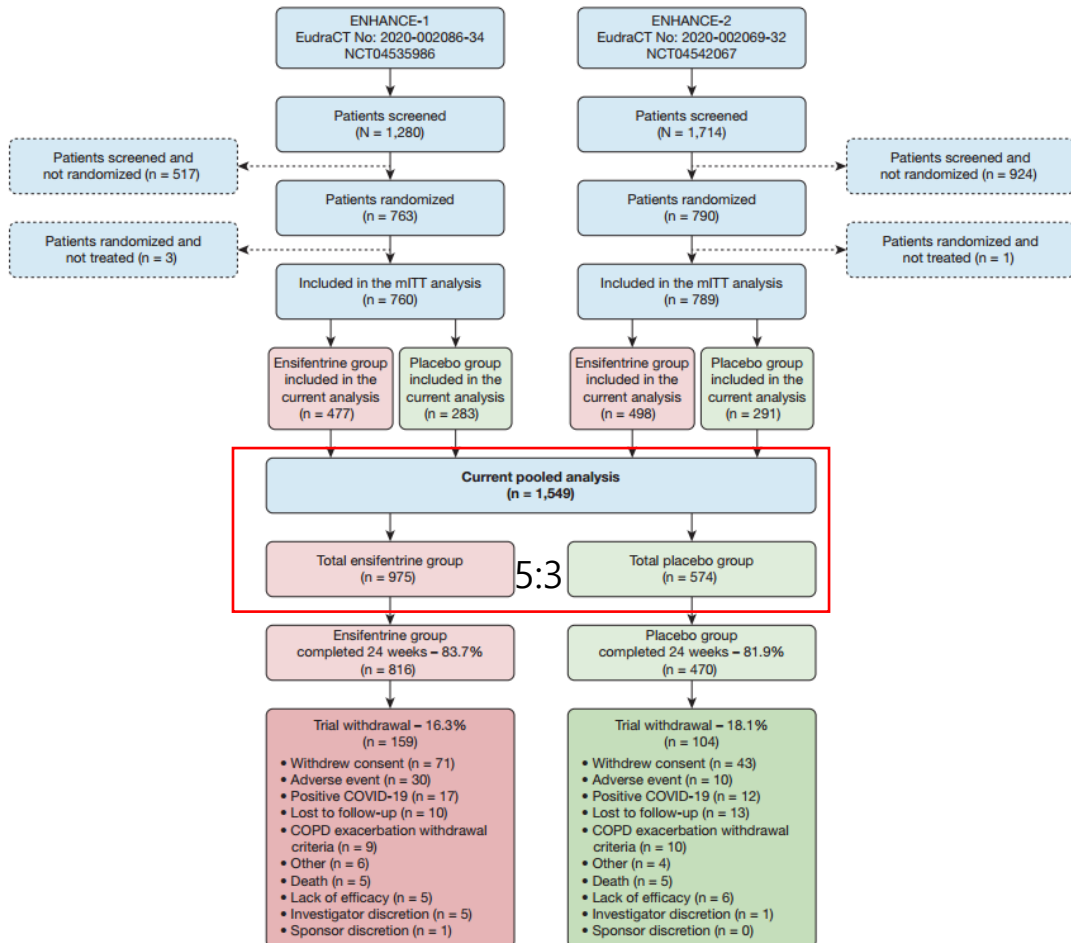
LABA + LAMA + Roflumilast effect "Broad, non-steroidal, anti-inflammatory effects"



# ExCOPD의 예방/치료 – (2-2) anti-inflammation

## Effect of Dual Phosphodiesterase 3 and 4 Inhibitor Ensifentrine on Exacerbation Rate and Risk in Patients With Moderate to Severe COPD

Frank C. Sciurba, MD; Stephanie A. Christenson, MD; Tara Rheault, PhD, MPH; Thomas Bengtsson, MSC; Kathleen Rickard, MD; and Igor Z. Barjaktarevic, MD, PhD



- **Methods and study populations**
  - phase 3, global, multicenter, randomized, double-blind, parallel-group, placebo-controlled clinical trials
  - 40-80yrs patients with symptomatic (mMRC $\geq$ 2) moderate to severe COPD
  - assigned randomly **5:3 to receive ensifentrine 3 mg bid or placebo over 24 weeks** via a standard jet nebulizer
  - Exclusion : Patients with asthma or a history of life-threatening COPD, recent hospitalizations for COPD, pneumonia/COVID-19 within 12 weeks or COPD exacerbation requiring oral or IV steroids within 3 months

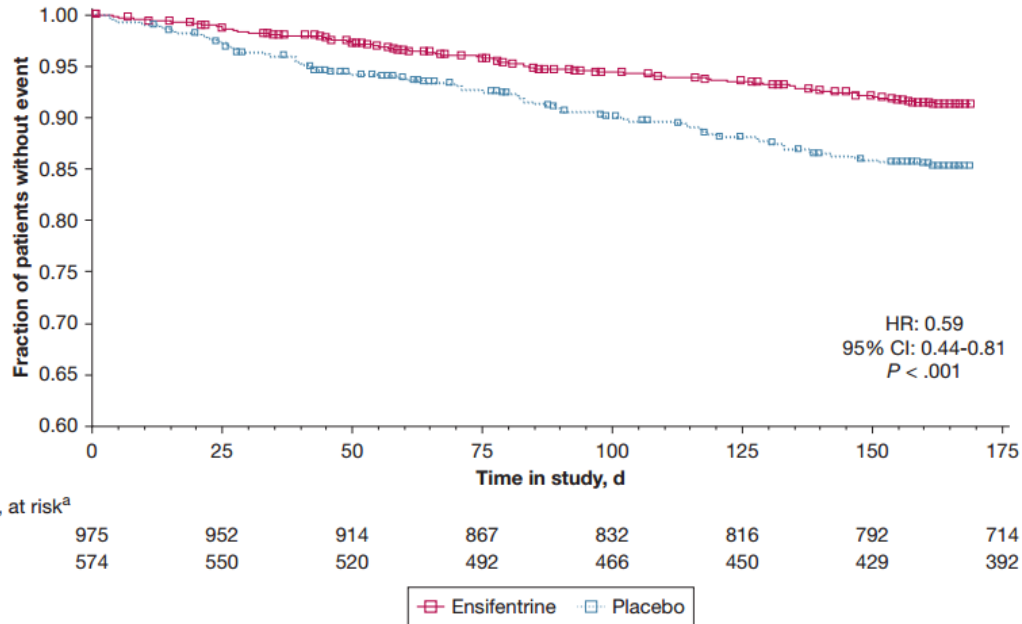
Characteristic	Pooled ENHANCE Trials	
	Ensifentrine Group (n = 975)	Placebo Group (n = 574)
Age, y	65	65
Sex, male	518 (53%)	305 (53%)
COPD severity		
Mild or moderate <sup>b</sup>	561 (58%)	307 (54%)
Severe or very severe <sup>b</sup>	414 (43%)	267 (47%)
FEV <sub>1</sub> , % predicted	51.8 (10.6)	51.0 (10.6)
Chronic bronchitis <sup>c</sup>	707 (73%)	405 (71%)
Current smoking history	544 (55%)	323 (56%)
Background medication(s)	606 (62%)	352 (61%)
LAMA	324 (33%)	171 (30%)
LABA	282 (29%)	181 (32%)
LABA plus ICS	159 (16%)	113 (20%)
Exacerbations in 15 mo before screening	220 (23%)	136 (24%)
Baseline assessment scores		
E-RS total	13.7 (6.7)	13.3 (6.1)
SGRQ total	49.4 (17.9)	49.1 (16.9)
BDI	5.9 (1.2)	5.9 (1.2)

Table 1. Demographic and Clinical Characteristics of the ENHANCE Pooled Modified Intention-to-Treat Population

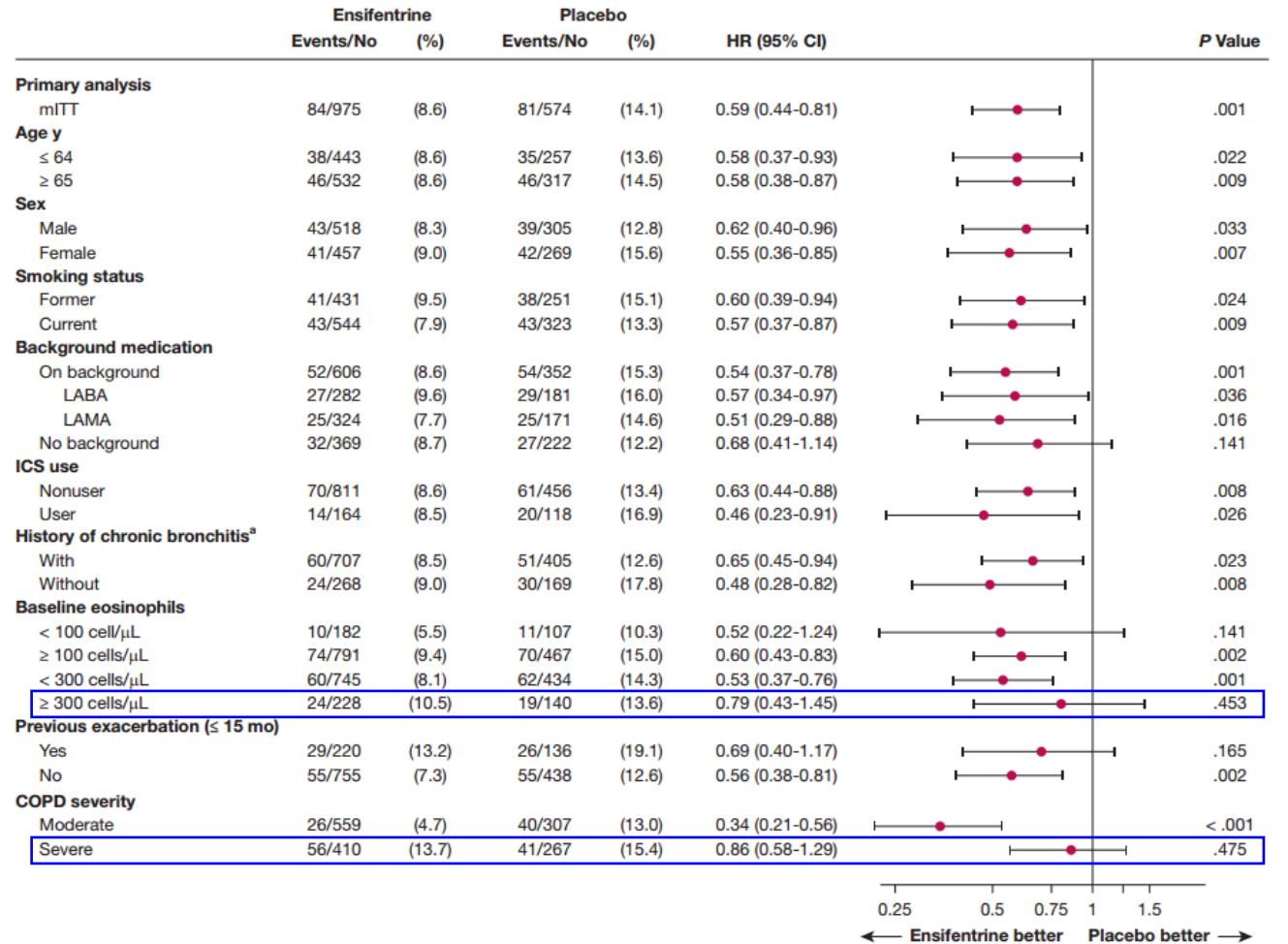


# ExCOPD의 예방/치료 – (2-2) anti-inflammation

Kaplan-Meier plot showing time to first moderate to severe COPD exacerbation over 24 weeks



Subgroup analysis. Forest plot showing HRs of time to first moderate to severe exacerbation by model covariate over 24 weeks



Eosinophil이 높지 않은 그룹에서 ensifentrine이 하나의 대안이 될 수 있다.



# ExCOPD의 예방/치료 – (3) Treatment factors

Original Article



## Predictors of Suboptimal Peak Inspiratory Flow in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease in Clinical Practice

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Peak inspiratory flow meter (incheck dial g16)



### \* Inclusion criteria

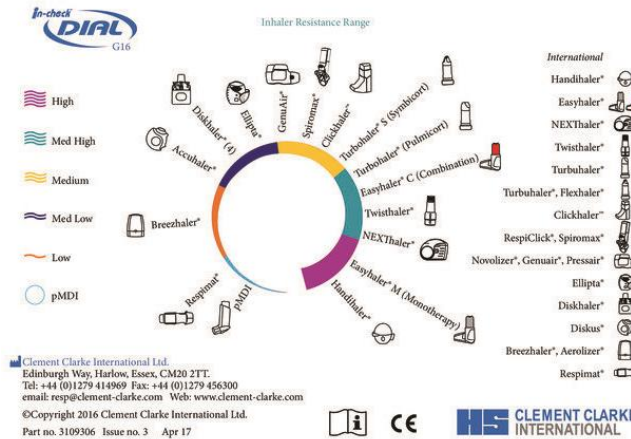
- 1) **72 patients** hospitalized for **acute exacerbation of COPD**
- 2) **received DPI therapy** as maintenance treatment prior to admission

### \* Exclusion criteria

current diagnoses of asthma, ILD, lung cancer, decompensated HF, and pneumonia, as well as cognitive impairments

### \* Peak inspiratory flow meter (PIF)

Optimal :  $\geq 60$  L/min  
Suboptimal :  $< 60$  L/min



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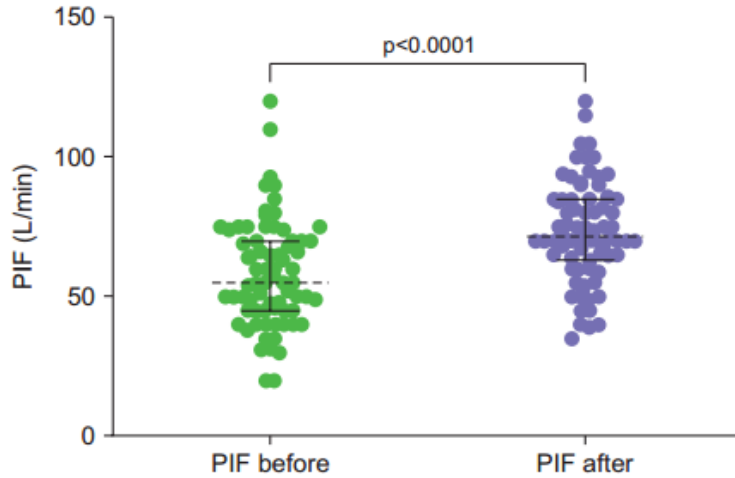
Parameter	Value
Age, yr	68.5 (63.0–72.8)
Sex, male/female, %	82/18
COPD, yr	4.5 (0.9–8.0)
BMI, kg/m <sup>2</sup>	26.1 (22.8–30.7)
Smoking history, pack/yr	40.0 (22.1–50.0)
mMRC, points	3 (3–4)
BCSS, points	5 (3–7)
CAT, points	25 (18–30)
SpO <sub>2</sub> , %	93 (92–95)
FVC, L	2.8 (2.2–3.5)
FVC, % pred.	74.5 (59.8–93.0)
FEV <sub>1</sub> , L	1.3 (0.8–1.8)
FEV <sub>1</sub> , % pred.	45.0 (29.0–63.0)
FEV <sub>1</sub> /FVC	0.5 (0.3–0.6)
IC, L	1.9 (1.4–2.2)
IC, % pred.	60.5 (50.8–72.3)
RV, L	3.2 (2.2–5.2)
RV, % pred.	139.0 (91.8–219.0)
RV/TLC, % pred.	50.3 (38.6–60.8)
ITGV, L	4.7 (3.1–5.9)
ITGV, % pred.	124.0 (92.5–159.8)
TLC, L	6.7 (5.2–8.3)
TLC, % pred.	100.0 (85.0–118.0)
DL <sub>CO</sub> , % pred.	45.0 (35.7–71.5)
MIP, % pred.	55.0 (41.5–72.5)
MEP, % pred.	95.0 (67.5–113.5)
CT (emphysema)	54 (75.0)
CT (bronchiectasis)	27 (28.0)

Parameter	Value
Type of inhaler	
Ellipta	33 (46%)
Breezhaler	25 (35%)
Turbuhaler	14 (19%)



# ExCOPD의 예방/치료 – (3) Treatment factors

**Figure 1.** Peak inspiratory flow (PIF) before and after the explanation of the adequate inhaler technique (at a resistance of patient's device used as the maintenance therapy).

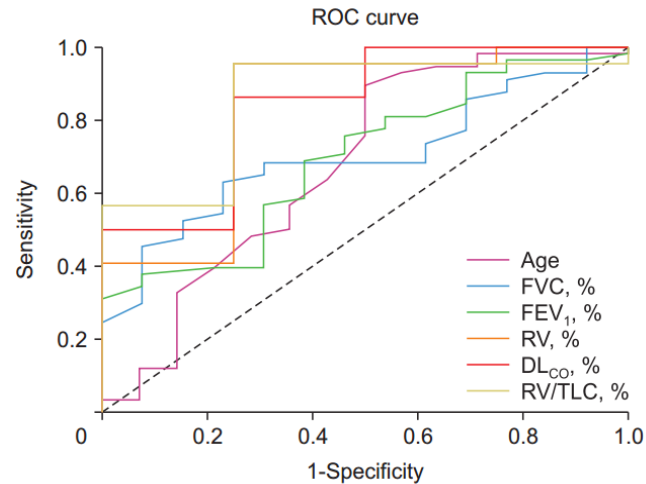


PIF : 55 L/min → 71.5 L/min  
 Suboptimal PIF : 38 (52.7%) → 14 (19.4%)

**Table 3.** Predictors of optimal PIF at admission

Parameter	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age, yr	0.91 (0.85–0.99)	0.023	0.89 (0.82–0.98)	0.02
FVC, L	3.33 (1.42–7.81)	0.006		
FVC,% pred.	1.04 (1.00–1.07)	0.032		
FEV <sub>1</sub> , L	4.85 (1.29–18.29)	0.024		
FEV <sub>1</sub> ,% pred.	1.04 (1.00–1.08)	0.038	1.08 (1.02–1.15)	0.009
RV, % pred.	0.98 (0.96–1.00)	0.047		
RV/TLC, %	0.89 (0.80–0.96)	0.040		

**Figure 3.** Receiver operating curve (ROC) curves to predict the optimal peak inspiratory flow at admission to the hospital. FVC: forced vital capacity; FEV<sub>1</sub>: forced expiratory volume in 1 second; RV: residual volume; DL<sub>CO</sub>: diffusing capacity for carbon monoxide; TLC: total lung capacity.



**ROC cut-off:**

- Age >70
- FVC <73% predicted
- FEV1 <35% predicted
- RV >194% predicted
- RV/TLC >70%
- DLCO <36% predicted

고령(>70), FEV1<35% 환자는 DPI 비적합 가능성이 높다  
 이 환자군은 DPI보다 pMDI + spacer 또는 nebulizer가 더 적절할 수 있음



# ExCOPD의 예방/치료 – (4) Comorbidities

JAMA Internal Medicine | Original Investigation

## Glucose-Lowering Medications and Risk of Chronic Obstructive Pulmonary Disease Exacerbations in Patients With Type 2 Diabetes

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### • Method

- 3개의 1:1 propensity score-matched 코호트 연구:
  - SGLT-2i vs DPP-4i (n=27,991)
  - GLP-1RA vs DPP-4i (n=32,107)
  - SGLT-2i vs GLP-1RA (n=36,218)
- 미국 3개 보험청구 데이터베이스(Optum, MarketScan, Medicare)를 사용

### • Study population : ≥40yrs, T2DM + active COPD 환자

Table 1. Selected Baseline Characteristics of Patients in the 1:1 PS-Matched Cohorts

Characteristic	1:1 PS-matched cohorts, No. (%)								
	SGLT-2i vs DPP-4i			GLP-1RA vs DPP-4i			SGLT-2i vs GLP-1RA		
	SGLT-2i (n = 27 991)	DPP-4i (n = 27 991)	Mean ASD	GLP-1RA (n = 32 107)	DPP-4i (n = 32 107)	Mean ASD	SGLT-2i (n = 36 218)	GLP-1RA (n = 36 218)	Mean ASD
Age, mean (SD), y	70.75 (8.62)	70.69 (8.79)	0.007	70.40 (8.49)	70.40 (8.18)	0.001	69.75 (8.72)	69.73 (8.68)	0.003
Sex									
Female	13 767 (49.2)	13 847 (49.5)	0.006	17 622 (54.9)	17 620 (54.9)	0.001	18 807 (51.9)	18 854 (52.1)	0.003
Race and ethnicity <sup>a</sup>									
Asian	280 (1.0)	300 (1.1)		225 (0.7)	321 (1.0)		398 (1.1)	326 (0.9)	
Black	2687 (9.6)	3107 (11.1)		3082 (9.6)	3789 (11.8)		3875 (10.7)	3694 (10.2)	
Hispanic	868 (3.1)	1026 (3.7)	0.061	899 (2.8)	1060 (3.3)	0.089	1304 (3.6)	1195 (3.3)	0.045
White	18 418 (65.8)	18 138 (64.8)		22 090 (68.8)	21 062 (65.6)		23 397 (64.6)	24 121 (66.6)	
Other/unknown/missing <sup>b</sup>	5738 (20.5)	5420 (19.4)		5811 (18.1)	5875 (18.3)		7244 (20.0)	6882 (19.1)	
Baseline HbA <sub>1c</sub> level, mean (SD), % <sup>c,d</sup>	7.87 (1.78)	7.97 (1.76)	0.020	8.1 (1.8)	8.1 (1.8)	0.002	8.0 (1.8)	8.0 (1.8)	0.009
Baseline lung parameters									
GOLD group E <sup>d</sup>	3104 (11.1)	3098 (11.1)	0.001	3675 (11.4)	3660 (11.4)	0.001	3954 (10.9)	3906 (10.8)	0.004
Glucocorticoids (oral)	12 933 (46.2)	12 830 (45.8)	0.007	14 709 (45.8)	14 682 (45.7)	0.002	16 753 (46.3)	16 767 (46.3)	0.001
Pneumonia	7034 (25.1)	7015 (25.1)	0.002	8142 (25.4)	8141 (25.4)	0.001	8580 (23.7)	8633 (23.8)	0.003
Asthma (active) <sup>e</sup>	3547 (12.7)	3594 (12.8)	0.005	4534 (14.1)	4476 (13.9)	0.005	4725 (13.0)	4762 (13.1)	0.003
Pulmonary hypertension	2763 (9.9)	2821 (10.1)	0.007	2965 (9.2)	3025 (9.4)	0.006	3438 (9.5)	3547 (9.8)	0.010
Pulmonary embolism	1472 (5.3)	1437 (5.1)	0.006	1796 (5.6)	1830 (5.7)	0.005	1990 (5.5)	1989 (5.5)	0.001
Obstructive sleep apnea or CPAP/BiPAP	8103 (28.9)	8141 (29.1)	0.002	9835 (30.6)	9836 (30.6)	0.001	12537 (34.6)	12530 (34.6)	0.001
Dual therapy <sup>f</sup>	12700 (45.4)	12754 (45.6)	0.002	14702 (45.8)	14817 (46.1)	0.007	16767 (46.3)	16723 (46.2)	0.002
Triple therapy <sup>g</sup>	1607 (5.7)	1632 (5.8)	0.001	1715 (5.3)	1766 (5.5)	0.007	2704 (7.5)	2728 (7.5)	0.003
Respiratory events during the 60 d before cohort entry									
Moderate or severe COPD exacerbation	1223 (4.4)	1233 (4.4)	0.002	1330 (4.1)	1320 (4.1)	0.002	1445 (4.0)	1460 (4.0)	0.002
Respiratory antibiotics	8442 (30.2)	8460 (30.2)	0.001	10 035 (31.3)	10 078 (31.4)	0.003	10 816 (29.9)	10 878 (30.0)	0.004
COPD hospitalization	697 (2.5)	705 (2.5)	0.002	784 (2.4)	753 (2.3)	0.006	725 (2.0)	748 (2.1)	0.004
Oxygen equipment use	3473 (12.4)	3528 (12.6)	0.006	3603 (11.2)	3663 (11.4)	0.006	5473 (15.1)	5477 (15.1)	0.001

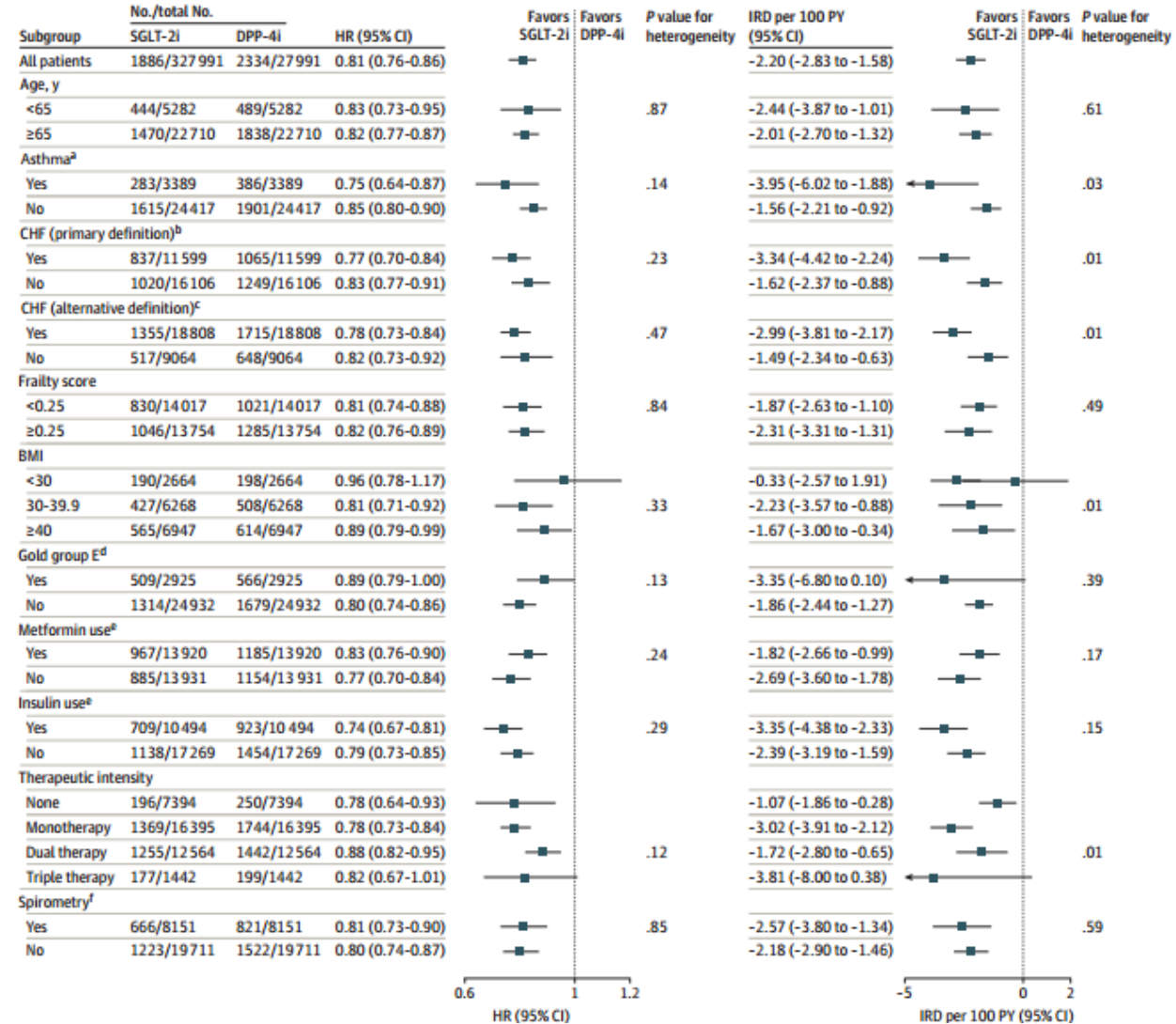
Comorbidities									
Obesity (BMI ≥30)	11 113 (39.7)	11 100 (39.7)	0.001	14 518 (45.2)	14 489 (45.1)	0.002	16 696 (46.1)	16 698 (46.1)	0.001
Combined comorbidity score, mean (SD)	5.31 (3.27)	5.27 (3.25)	0.012	5.46 (3.20)	5.46 (3.22)	0.002	5.19 (3.14)	5.21 (3.13)	0.005
Frailty score									
<0.15	1211 (4.3)	1218 (4.4)	0.005	1074 (3.3)	1072 (3.3)	0.003	1481 (4.1)	1489 (4.1)	0.002
0.15-0.25	12 826 (45.8)	12 885 (46.0)		13 245 (41.3)	13 285 (41.4)		16 953 (46.8)	16 967 (46.8)	
≥0.25	13 954 (49.9)	13 888 (49.6)		17 788 (55.4)	17 750 (55.3)		17 784 (49.1)	17 762 (49.0)	
Diabetic retinopathy	10 626 (38.0)	10 524 (37.6)	0.008	12 714 (39.6)	12 743 (39.7)	0.002	14 766 (40.8)	14 820 (40.9)	0.003
Diabetic neuropathy	9360 (33.4)	9301 (33.2)	0.004	11 541 (35.9)	11 547 (36.0)	0.001	13 218 (36.5)	13 181 (36.4)	0.002
Peripheral vascular disease/surgery	7352 (26.3)	7224 (25.8)	0.010	8729 (27.2)	8724 (27.2)	0.001	9146 (25.3)	9141 (25.2)	0.001
Congestive heart failure	12 352 (44.1)	12 237 (43.7)	0.008	14 239 (44.3)	14 127 (44.0)	0.007	15 671 (43.3)	15 725 (43.4)	0.003
CKD stage 1-2	1549 (5.5)	1532 (5.5)	0.003	1757 (5.5)	1701 (5.3)	0.008	2052 (5.7)	2038 (5.6)	0.002
Other medications									
Insulins (concurrent use) <sup>h</sup>	10 741 (38.4)	10 595 (37.9)	0.011	15 672 (48.8)	15 632 (48.7)	0.002	15 637 (43.2)	15 677 (43.3)	0.002
Sulfonylureas (second generation)	10 083 (36.0)	10 003 (35.7)	0.006	11 266 (35.1)	11 307 (35.2)	0.003	13 163 (36.3)	13 003 (35.9)	0.009
Metformin (concurrent use) <sup>h</sup>	13 860 (49.5)	13 873 (49.6)	0.001	14 321 (44.6)	14 357 (44.7)	0.002	16 545 (45.7)	16 593 (45.8)	0.003
GLP-1RA	3095 (11.1)	2894 (10.3)	0.023	NA	NA	NA	NA	NA	NA
SGLT-2i	NA	NA	NA	3052 (9.5)	3131 (9.8)	0.008	NA	NA	NA
DPP-4i	NA	NA	NA	NA	NA	NA	9107 (25.1)	9058 (25.0)	0.003
Thiazolidinediones	1853 (6.6)	1916 (6.8)	0.009	1957 (6.1)	1994 (6.2)	0.005	2464 (6.8)	2462 (6.8)	0.001
Health care utilization, mean (SD)									
No. of hospitalizations	1.21 (1.58)	1.20 (1.52)	0.009	1.24 (1.55)	1.24 (1.56)	0.001	1.09 (1.46)	1.09 (1.53)	0.001
No. of pulmonologist visits	1.93 (4.46)	1.94 (3.95)	0.001	1.96 (4.06)	1.93 (4.38)	0.006	1.83 (4.05)	1.83 (3.97)	0.001
Influenza vaccination	14 229 (50.8)	14 142 (50.5)	0.006	16 786 (52.3)	16 781 (52.3)	0.001	18 117 (50.0)	18 124 (50.0)	0.001
Socioeconomic status parameters, mean (SD)									
Ratio of unique brand to generic medicines	1.03 (0.04)	1.03 (0.04)	0.002	1.03 (0.04)	1.03 (0.04)	0.003	1.03 (0.04)	1.03 (0.04)	0.001



# ExCOPD의 예방/치료 – (4) Comorbidities

Table 2. First Chronic Obstructive Pulmonary Disease Exacerbation in the 1:1 Propensity Score-Matched Cohorts

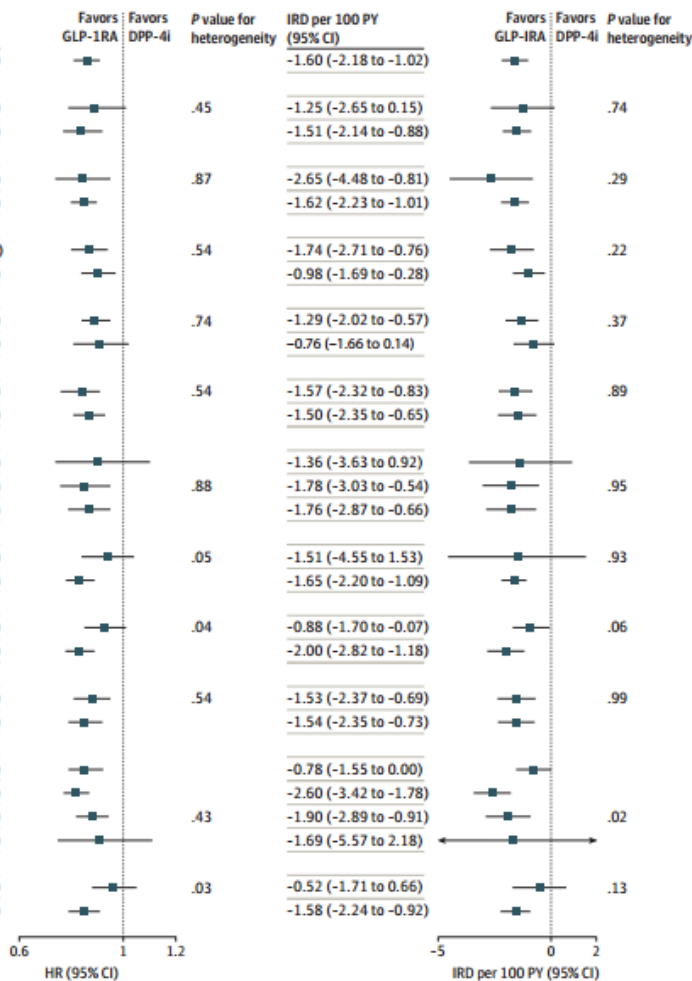
Parameters	SGLT-2i vs DPP-4i		GLP-1RA vs DPP-4i		SGLT-2i vs GLP-1RA	
	SGLT-2i (n = 27 991)	DPP-4i (n = 27 991)	GLP-1RA (n = 32 107)	DPP-4i (n = 32 107)	SGLT-2i (n = 36 218)	GLP-1RA (n = 36 218)
<b>Moderate or severe exacerbation</b>						
No. of events	1886	2334	2365	2829	2363	2525
Follow-up time, median (IQR), d	145 (61 to 335)	147 (62 to 336)	142 (63 to 339)	156 (66 to 355)	141 (61 to 316)	139 (65 to 314)
IR/100 PYs	9.26	11.44	9.89	11.49	9.47	10.00
IRD/100 PYs (95% CI)	-2.20 (-2.83 to -1.58)		-1.60 (-2.18 to -1.02)		-0.55 (-1.09 to -0.01)	
HR (95% CI)	0.81 (0.76 to 0.86)		0.86 (0.81 to 0.91)		0.94 (0.89 to 1.00)	
<b>Severe exacerbation</b>						
No. of events	842	1201	1195	1510	1025	1121
Follow-up time, median (IQR), d	150 (67 to 354)	155 (69 to 356)	147 (69 to 356)	164 (73 to 377)	147 (67 to 329)	144 (70 to 331)
IR/100 PYs	3.95	5.61	4.79	5.84	3.94	4.24
IRD/100 PYs (95% CI)	-1.42 (-1.81 to -1.03)		-1.06 (-1.46 to -0.65)		-0.35 (-0.68 to -0.02)	
HR (95% CI)	0.71 (0.65 to 0.78)		0.82 (0.76 to 0.89)		0.93 (0.85 to 1.01)	



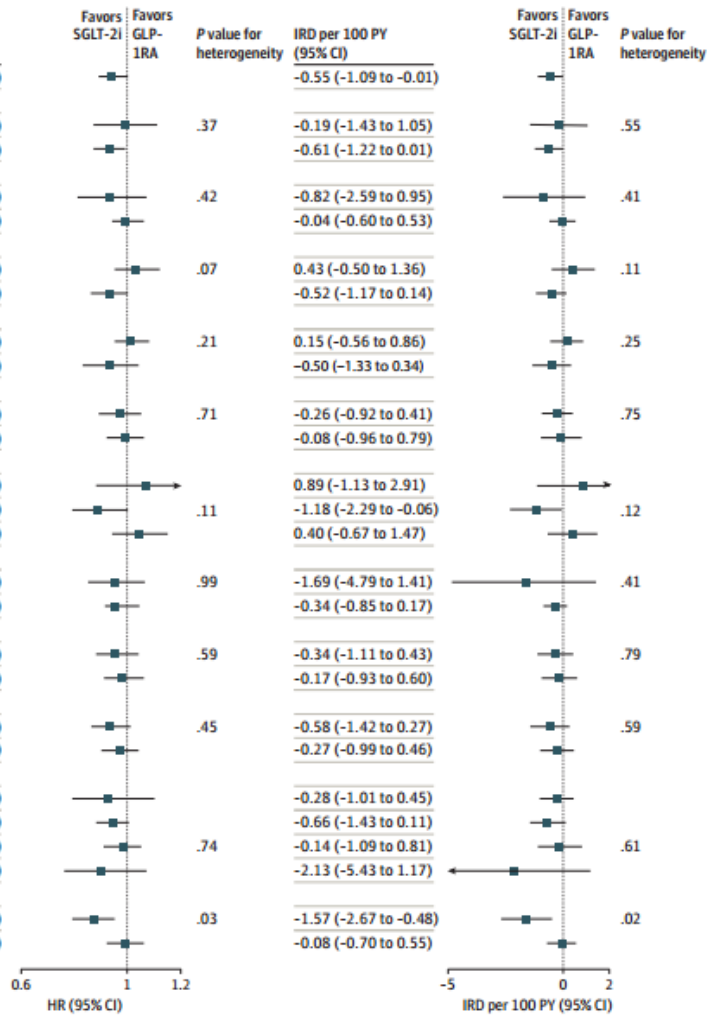


# ExCOPD의 예방/치료 – (4) Comorbidities

Subgroup	No./total No.		HR (95% CI)
	GLP-1RA	DPP-4i	
All patients	2525/32107	2669/32107	0.86 (0.81-0.91)
Age, y			
<65	495/5740	539/5740	0.89 (0.79-1.01)
≥65	1896/26720	2283/26720	0.84 (0.77-0.92)
Asthma <sup>a</sup>			
Yes	432/4334	521/4334	0.84 (0.74-0.95)
No	1909/27604	2316/27604	0.85 (0.80-0.90)
CHF (primary definition) <sup>b</sup>			
Yes	1114/14030	1309/14030	0.87 (0.80-0.94)
No	1239/17936	1431/17936	0.90 (0.84-0.97)
CHF (alternative definition) <sup>c</sup>			
Yes	1871/23010	2128/23010	0.89 (0.84-0.95)
No	556/9351	648/9351	0.91 (0.81-1.02)
Frailty score			
<0.25	837/14103	1043/14103	0.84 (0.76-0.91)
≥0.25	1475/17838	1747/17838	0.87 (0.81-0.93)
BMI			
<30	177/2435	198/2435	0.90 (0.74-1.10)
30-39.9	558/7445	655/7445	0.85 (0.76-0.95)
≥40	831/9428	915/9428	0.87 (0.79-0.95)
Gold group E <sup>d</sup>			
Yes	641/3514	704/3514	0.94 (0.84-1.04)
No	1690/28443	2112/28443	0.83 (0.78-0.89)
Metformin use <sup>e</sup>			
Yes	1109/14350	1233/14350	0.93 (0.85-1.01)
No	1275/17735	1565/17735	0.83 (0.78-0.89)
Insulin use <sup>e</sup>			
Yes	1245/15603	1393/15603	0.88 (0.81-0.95)
No	1106/16182	1396/16182	0.85 (0.79-0.92)
Therapeutic intensity			
None	237/8264	299/8264	0.85 (0.79-0.92)
Monotherapy	1777/19337	2182/19337	0.82 (0.77-0.87)
Dual therapy	1582/14683	1791/14683	0.88 (0.82-0.94)
Triple therapy	181/1538	201/1538	0.91 (0.75-1.11)
Spirometry <sup>f</sup>			
Yes	910/9407	964/9407	0.96 (0.88-1.05)
No	1491/22613	1820/22613	0.85 (0.79-0.91)



Subgroup	No./total No.		HR (95% CI)
	SGLT-2i	GLP-1RA	
All patients	2363/36218	2525/36218	0.94 (0.89-1.00)
Age, y			
<65	612/7890	608/7890	0.99 (0.87-1.11)
≥65	1761/28126	1906/28126	0.93 (0.87-0.99)
Asthma <sup>a</sup>			
Yes	362/4473	401/4473	0.93 (0.81-1.07)
No	1987/31516	2013/31516	0.99 (0.94-1.06)
CHF (primary definition) <sup>b</sup>			
Yes	1123/15250	1081/15250	1.03 (0.95-1.12)
No	1218/20406	1333/20406	0.93 (0.86-1.00)
CHF (alternative definition) <sup>c</sup>			
Yes	1827/24908	1814/24908	1.01 (0.95-1.08)
No	626/11287	672/11287	0.93 (0.83-1.04)
Frailty score			
<0.25	1031/18245	1055/18245	0.97 (0.89-1.05)
≥0.25	1335/17628	1385/17628	0.99 (0.92-1.06)
BMI			
<30	207/3045	191/3045	1.07 (0.88-1.31)
30-39.9	549/8959	615/8959	0.89 (0.79-1.00)
≥40	748/10587	760/10587	1.04 (0.94-1.15)
Gold group E <sup>d</sup>			
Yes	606/3632	640/3632	0.95 (0.85-1.06)
No	1704/32352	1799/32352	0.95 (0.89-1.02)
Metformin use <sup>e</sup>			
Yes	1097/16498	1155/16498	0.95 (0.88-1.04)
No	1263/19387	1287/19387	0.98 (0.91-1.06)
Insulin use <sup>e</sup>			
Yes	1010/15496	1111/15496	0.93 (0.86-1.01)
No	1327/20191	1354/20191	0.97 (0.90-1.04)
Therapeutic intensity			
None	259/9272	265/9272	0.93 (0.79-1.10)
Monotherapy	1673/21046	1820/21046	0.94 (0.88-1.00)
Dual therapy	1548/16474	1633/16474	0.98 (0.91-1.05)
Triple therapy	257/2392	272/2392	0.90 (0.76-1.07)
Spirometry <sup>f</sup>			
Yes	833/10681	956/10681	0.87 (0.79-0.95)
No	1528/25339	1555/25339	0.99 (0.92-1.06)



DPP4 inhibitor 보다는 GLP-1Rc agonist 나 SGLT inhibitor가 Moderate to severe exacerbation을 더 감소시키는 경향이 있더라.

# Take Home message

## 1. COPD Exacerbation의 진단 & 예측인자

- 1) Blood lab : serum IgG – 정상범위라도 낮을수록 COPDEx ↑
- 2) CT images : Airway mucus plug, emphysema - COPDEx ↑
- 3) Pulmonary pressure : High TR gradient - Day alive and out of hospital ↓

## 2. COPD Exacerbation의 원인

- 1) Infection
- 2) Eosinophil/systemic inflammation
- 3) Treatment related factor
- 4) Comorbidities

## 3. COPD Exacerbation의 예방 & 치료

- 1) Infection – Vaccination (RSV, Covid)
- 2) Eosinophil inflammation – Dupilumab, Mepolizumab, Benralizumab
- 3) Non eosinophilic inflammation - Ensifentrine
- 4) Treatment related factor – optimal PIF, 고령(>70), FEV1<35%, RV 증가 환자는 DPI 비적합 가능성
- 5) Comorbidities – DM control (GLP-1Rc agonist & SGLT inhibitor more favorable than DPP4 inhibitor)



**Thank you**