2019台灣胸腔暨重症加護醫學會夏季會
2019 Summer Workshop of Taiwan Society of Pulmonary and Critical Care Medicine

Pharmacological Withdrawal for COPD

羅東博愛醫院
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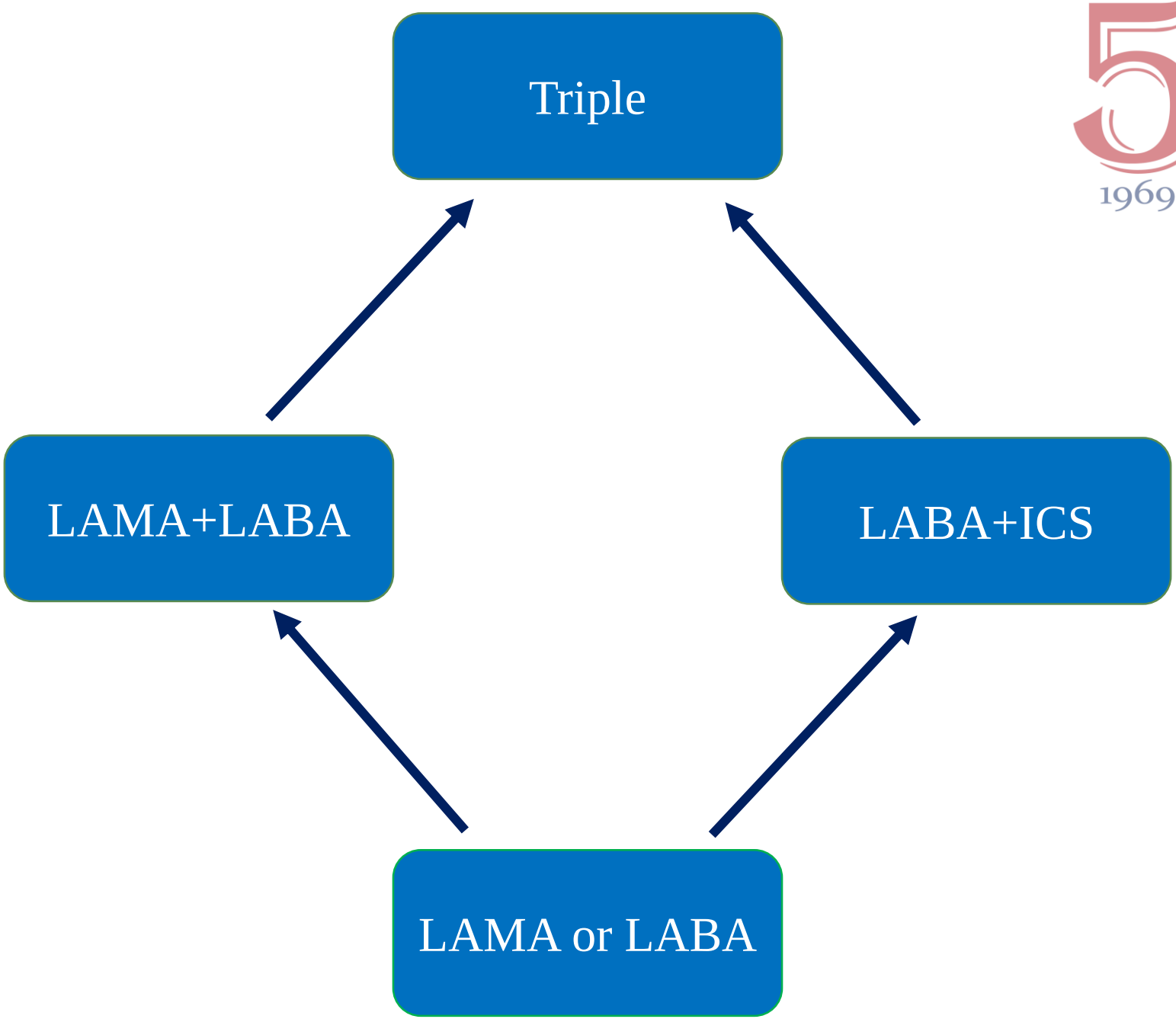
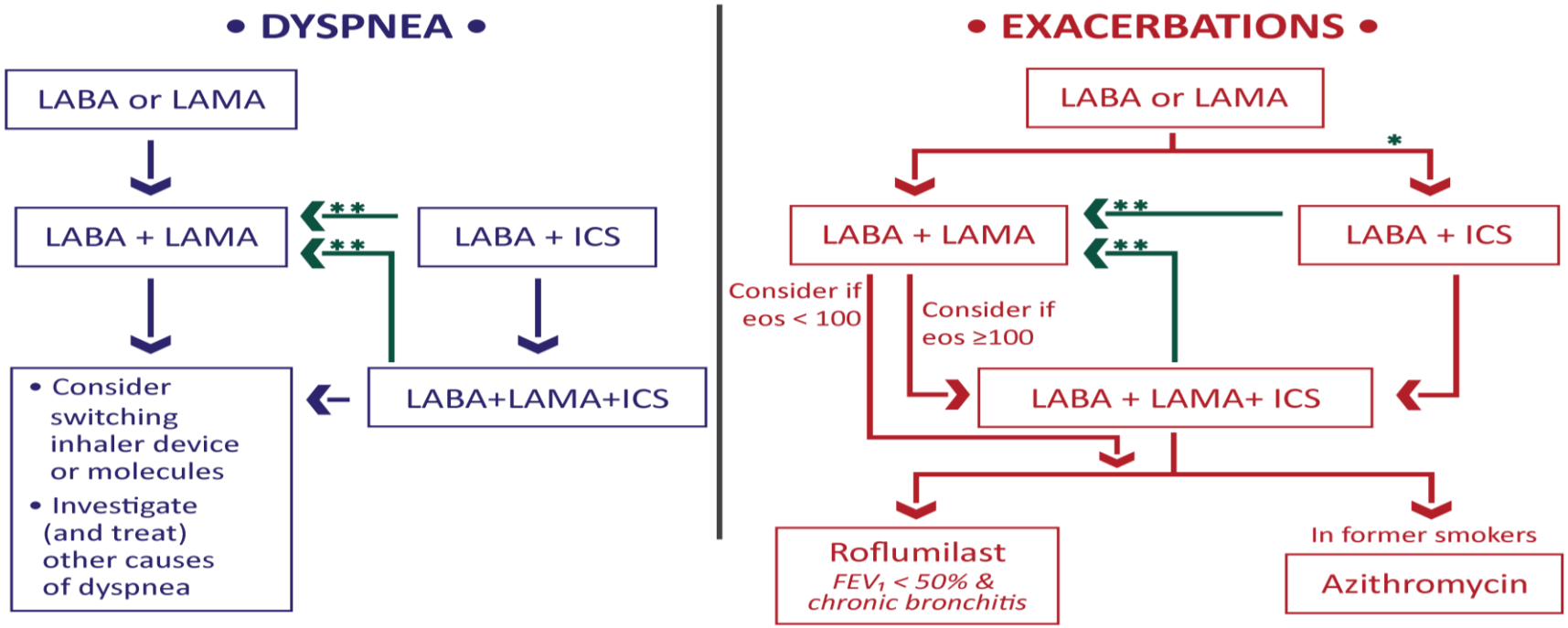

Triple
LAMA+LABA
LABA+ICS
LAMA or LABA

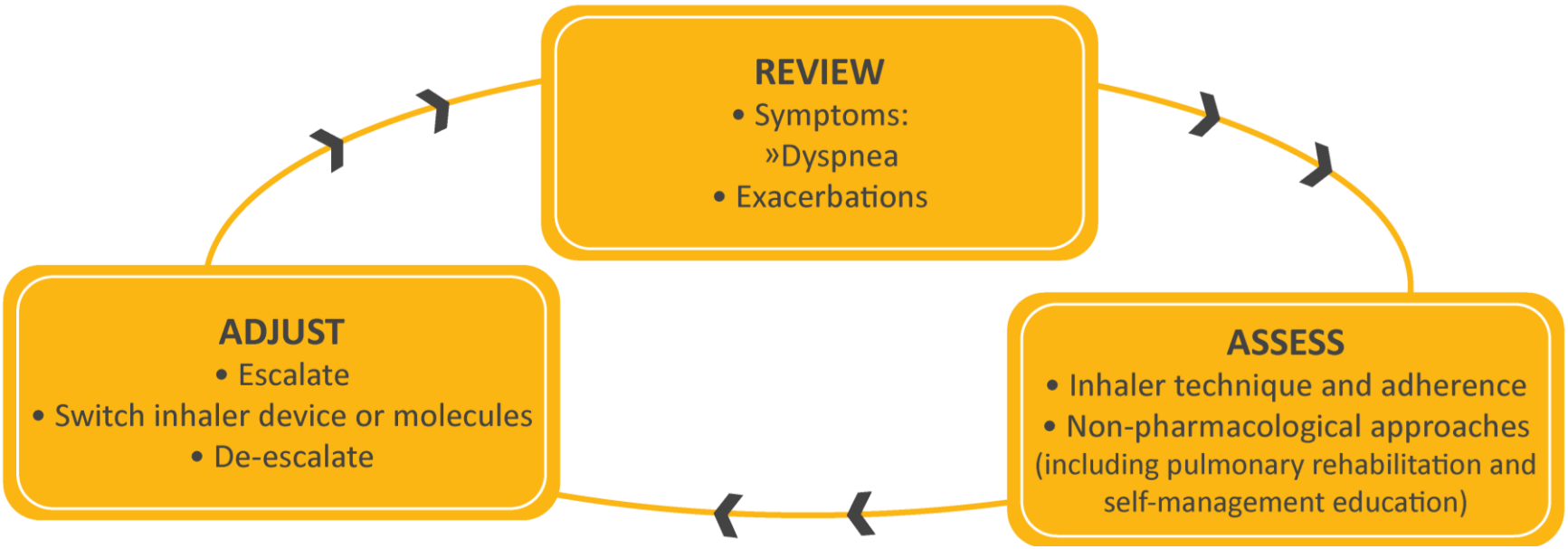
Follow-up Treatment

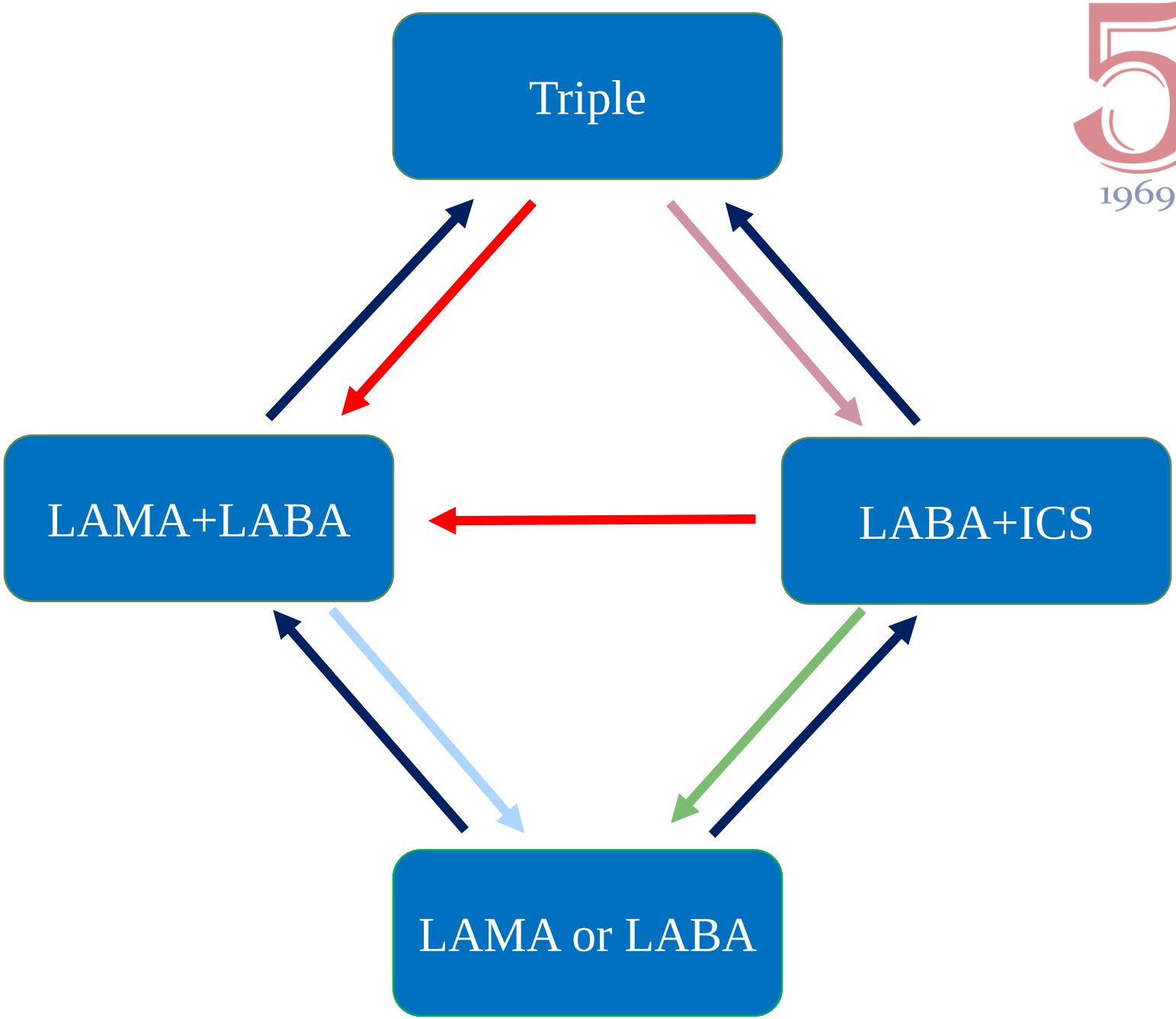
1. **IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.**
2. **IF NOT:**
   - ✓ Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - ✓ Place patient in box corresponding to current treatment & follow indications
   - ✓ Assess response, adjust and review
   - ✓ These recommendations do not depend on the ABCD assessment at diagnosis



eos = blood eosinophil count (cells/µL)
** Consider if eos ≥ 300 or eos ≥ 100 AND ≥2 moderate exacerbations / 1 hospitalization*
*** Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS*

Management Cycle




Triple
LAMA+LABA
LABA+ICS
LAMA or LABA

- 1. ICS tapering
- 2. Dual therapy → monotherapy
- 3. Triple therapy → combination therapy

COPE study

A randomized, single center, double-blind, placebo controlled study

244 COPD patients prescribed with ICS +SAMA for 4 months

FP

6 months

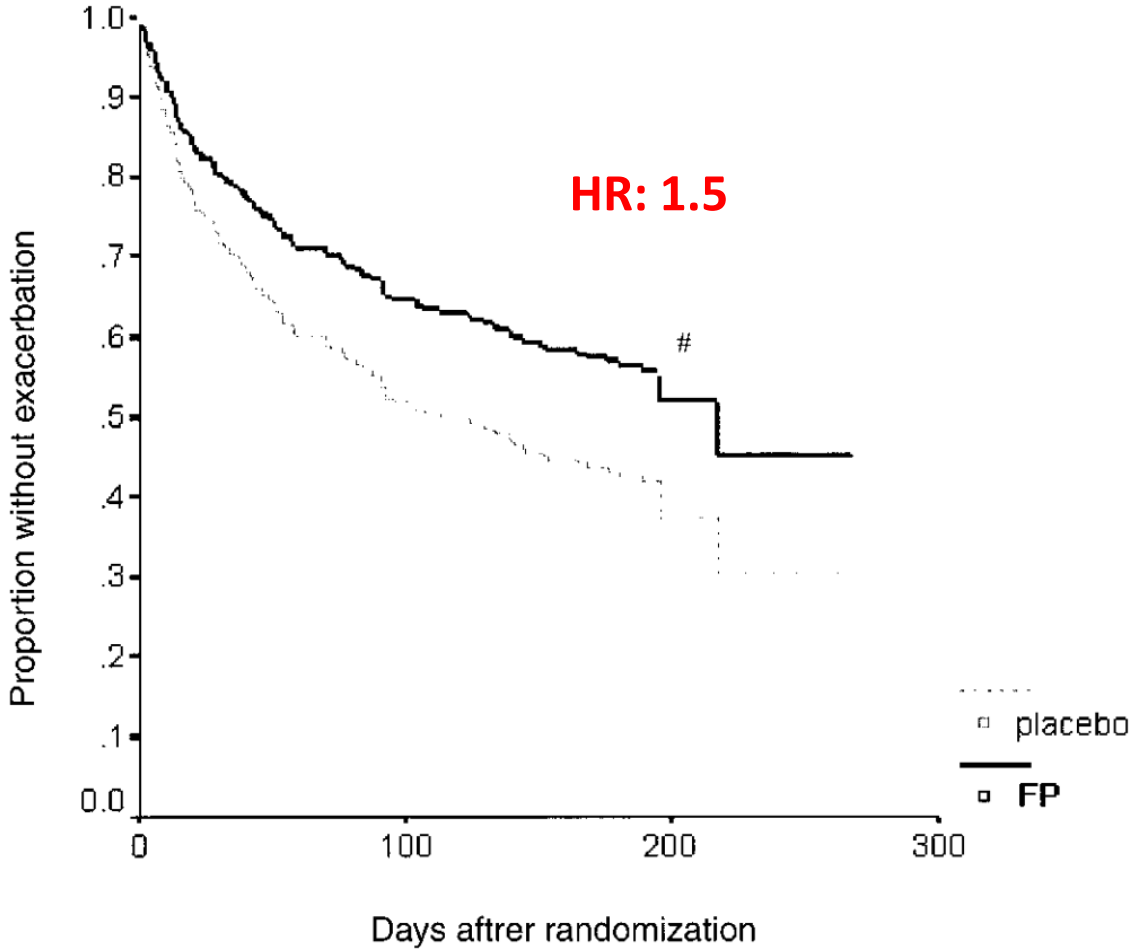
Placebo

Exacerbation

Patients: Pre-FEV1 25-80%
Pre FEV1/FVC< 60%
No airway reversibility
1.3 AE in the preceding year
83% ICS use
46% LABA use

Am J Respir Crit Care Med Vol 166. pp 1358–1363, 2002

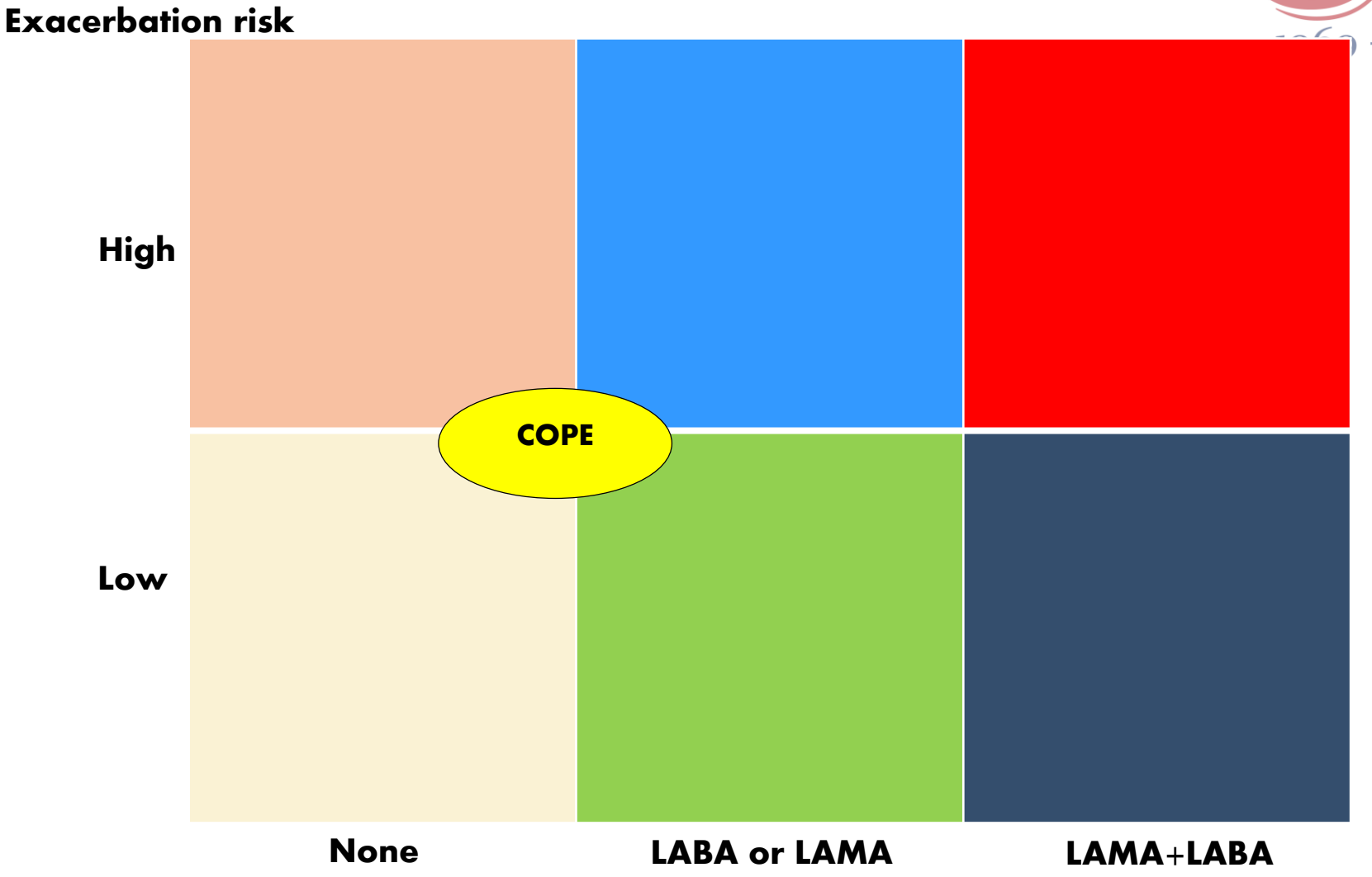
Discontinuation of FP led to a more rapid onset and higher risk of exacerbations



FEV1↘ 38cc/6M

Outcome Parameter	FP (*Mean* ± *SE*)	Placebo (*Mean* ± *SE*)	Difference* (*95% CI*)
Change in FEV_1 after bronchodilator, ml	−4.6 ± 1.6 (n = 122)	−22.9 ± 1.7 (n = 120)	38 (−79.5; 1.6)†
Six minute walk, m	−11.0 ± 4.8 (n = 87)‡	−0.2 ± 5.2 (n = 85)‡	9.37 (−4.47; 23.21)§
Change in Borg score, units	−0.07 ± 0.2 (n = 88)‡	−0.29 ± 0.2 (n = 85)‡	0.29 (−0.13; 0.71)§

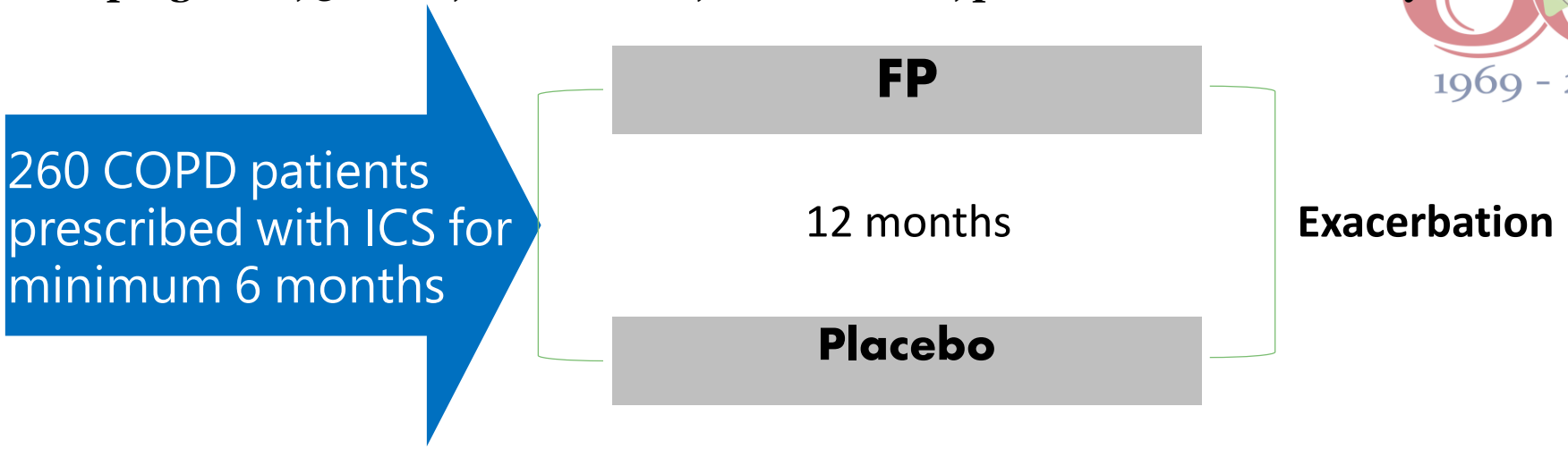
Withdrawn of ICS on exacerbations



Modified from IJCOPD 2018:13 2089–2099

WISP trial

A pragmatic, 36LMD, randomized, double-blind, placebo controlled study



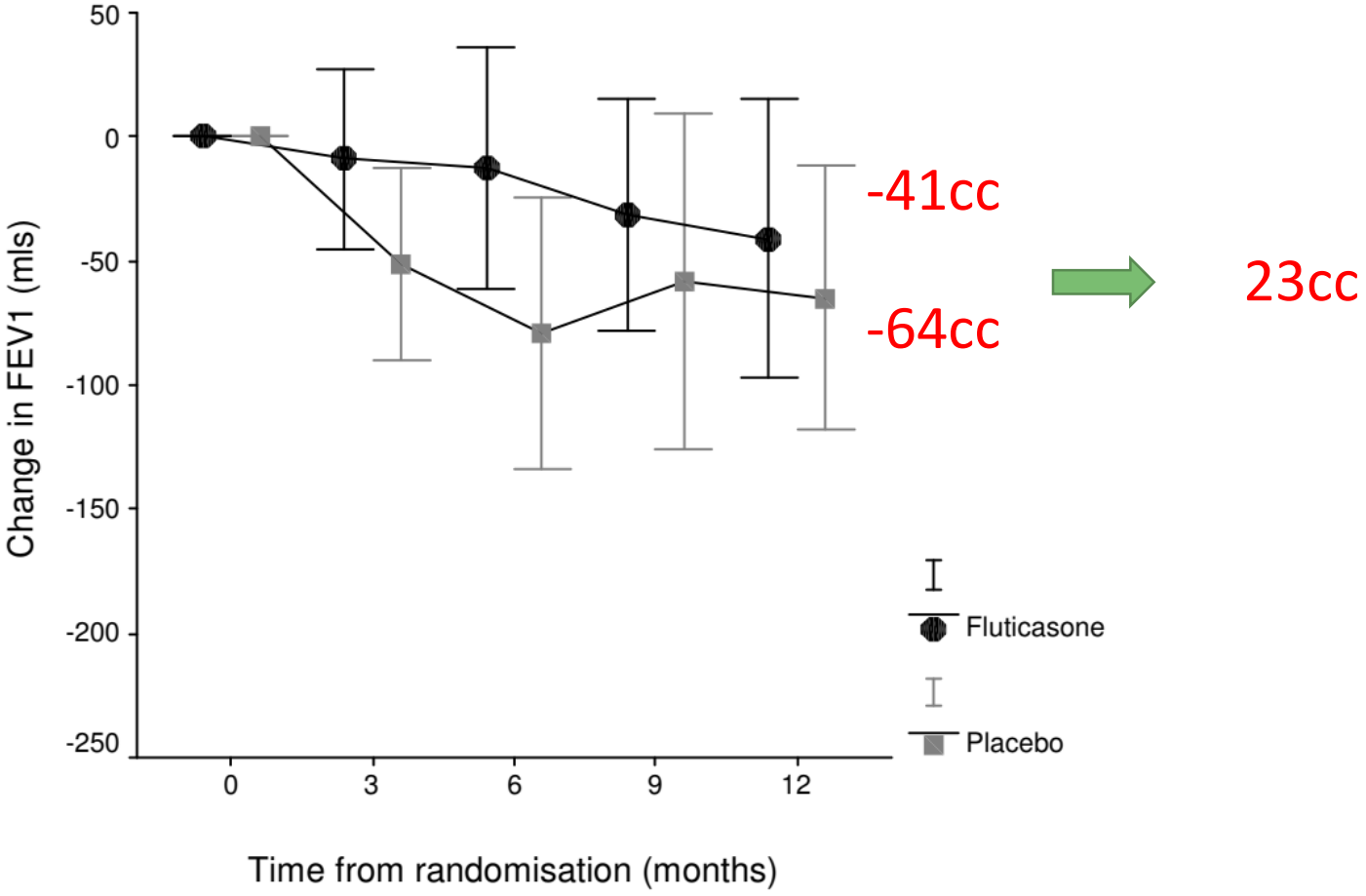
Patients: Post-FEV1/FVC< 70%
FEV1 < 80%
Reversibility <15% or 200cc
Mean number of exacerbation: 1.5/yr
ICS use > 8yrs
LABA use 33%

Respiratory Research 2007, **8**:93

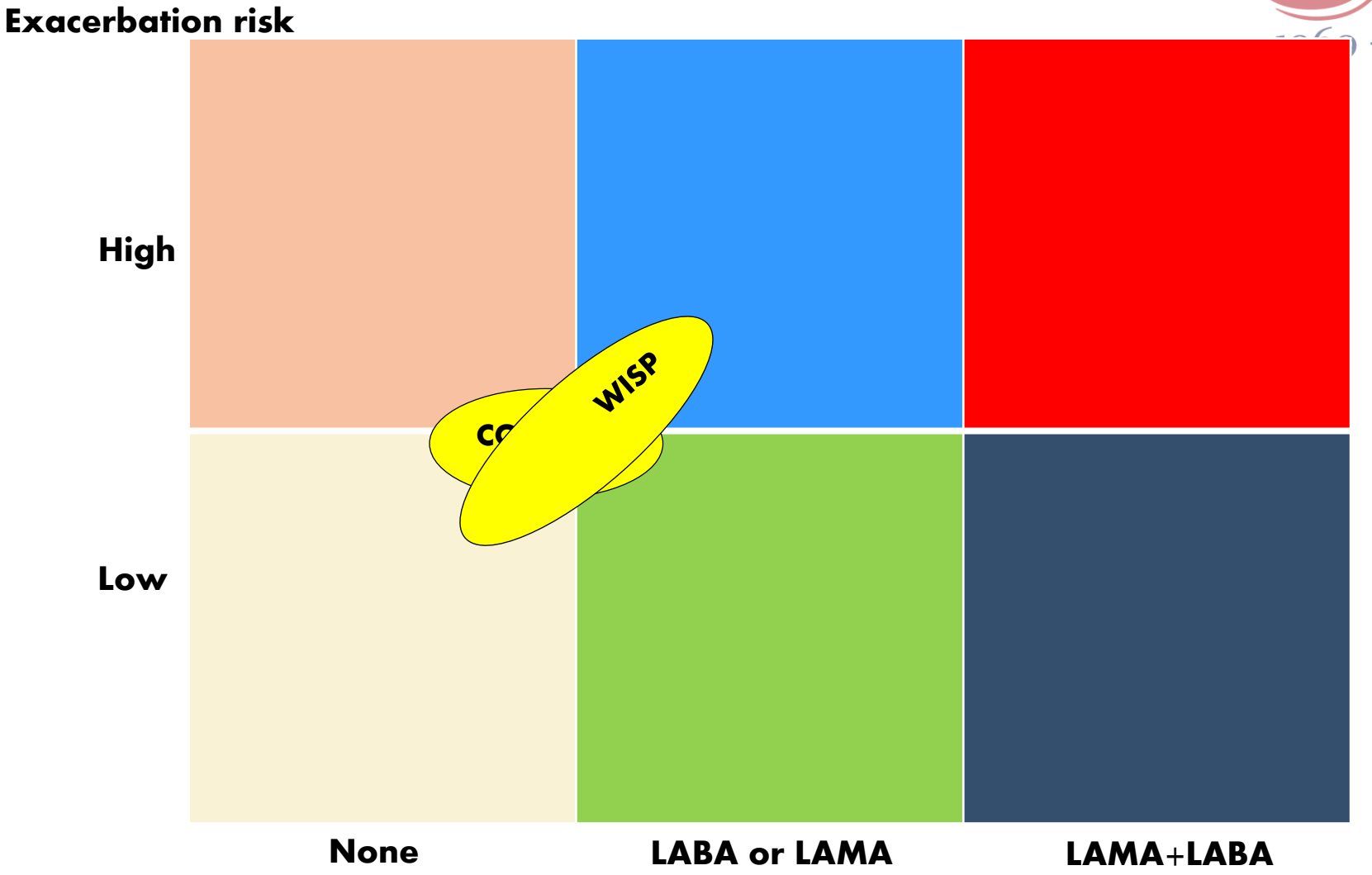
	COPD exacerbations				Relative risk of COPD exacerbation for patients randomised to placebo or fluticasone (n = 260)			
	Fluticasone (n = 128)		Placebo (n = 132)		Exacerbation grouping	Incidence rate ratio	95% confidence interval		adjusted p-value
Exacerbations while in trial	Unreported	129	Unreported	116	All	**1.11**	0.91	1.36	0.298
	Moderate	224	Moderate	276					
	Severe	21	Severe	22	Moderate and severe only	**1.25**	0.96	1.58	0.067
	Total	**373**	**Total**	**413**					
Exacerbations while on randomised treatment	Unreported	112	Unreported	99	All	**1.48**	1.17	1.86	0.001
	Moderate	158	Moderate	182					
	Severe	9	Severe	12	Moderate and severe only	**1.63**	1.23	2.17	0.001
	Total	**279**	**Total**	**293**					

In patients with worse COPD, ICS+ LABA were prescribed for them. The AE risk for ICS withdrawal was 1.24 (CI 0.96-1.41)

FEV1 decline



Withdrawn of ICS on exacerbations



Modified from IJCOPD 2018:13 2089–2099

COSMIC study

A randomized, 39 centers, double-blind, placebo controlled study

373 COPD patients prescribed with ICS+LABA for 3 months

FP+Salmeterol

12 months

Salmeterol

Exacerbation

Patients: Pre-FEV1 30~70%
FEV1/FVC<88%
No airway reversibility
2 AE in the preceding year

Thorax 2005;60:480–487

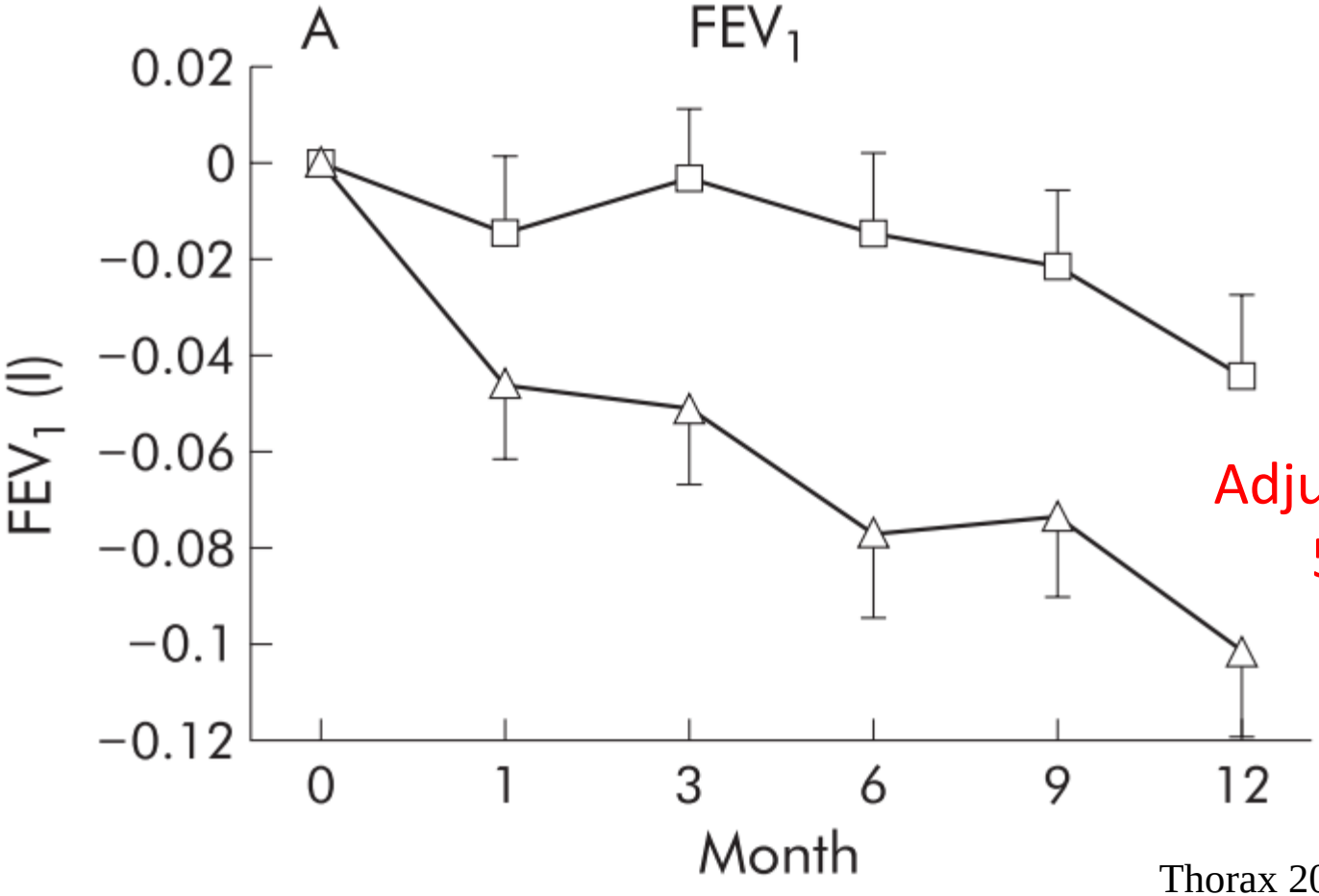
Only mild AE is increased

	S	SFC	Rate ratio
Total AE	254	238	1.067
Mild AE /yr	1.6	0.6	2.6 *
Moderate to Severe AE /yr	1.6	1.3	1.2 (0.9~1.5)

FEV1 change after ICS withdrawal

Δ : salmeterol

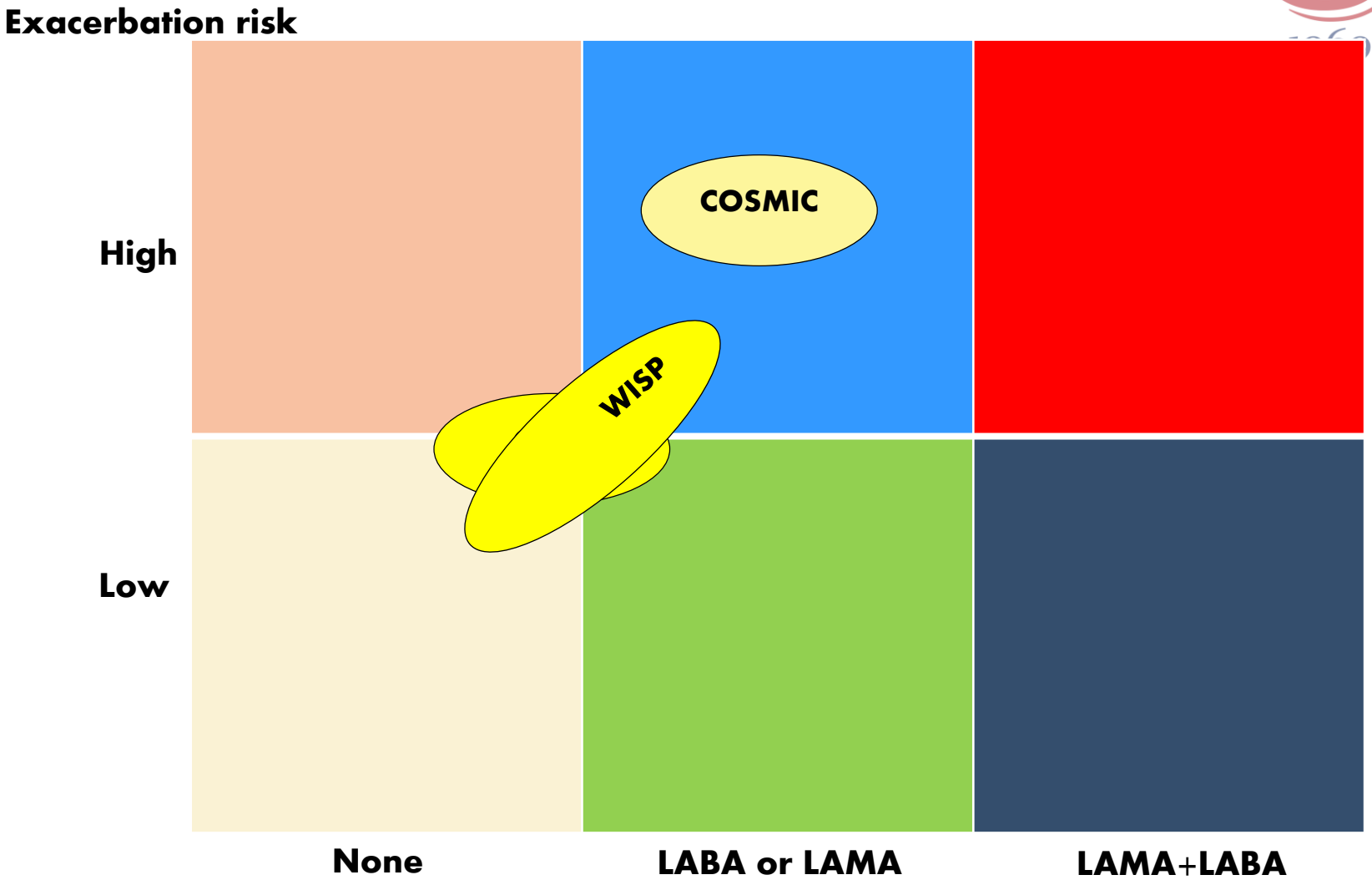
□: Salmeterol+ fluticasone



Adjusted ΔFEV1↘
50cc/12M

Thorax 2005;60:480–487

Withdrawn of ICS on exacerbations



Modified from IJCOPD 2018:13 2089–2099

INSTEAD study

A randomized, multinational, double-blind, double-dummy phase IV study

581 COPD patients prescribed with SFC for 3 months

Patients: 50%≤ FEV1 <80%
0 COPD exacerbation

SFC 50/500

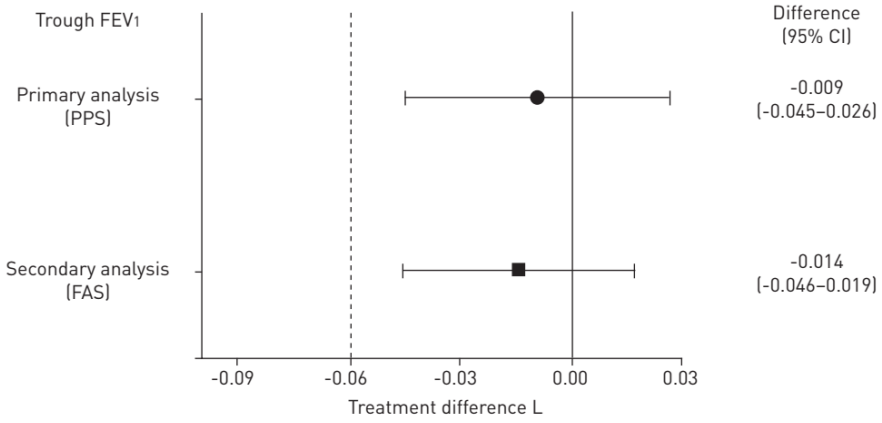
12 wks

IND 150ug

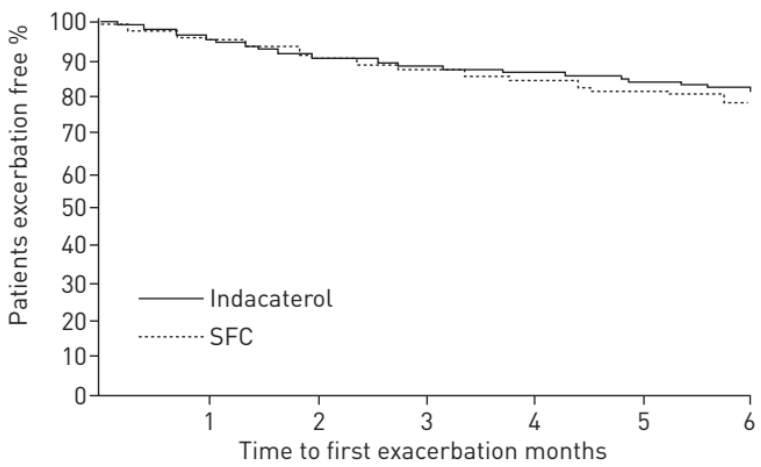
non-inferiority on FEV1
AE....

Eur Respir J. 2014 Dec;44(6):1548-56

No difference between Trough FEV1 and Exacerbation

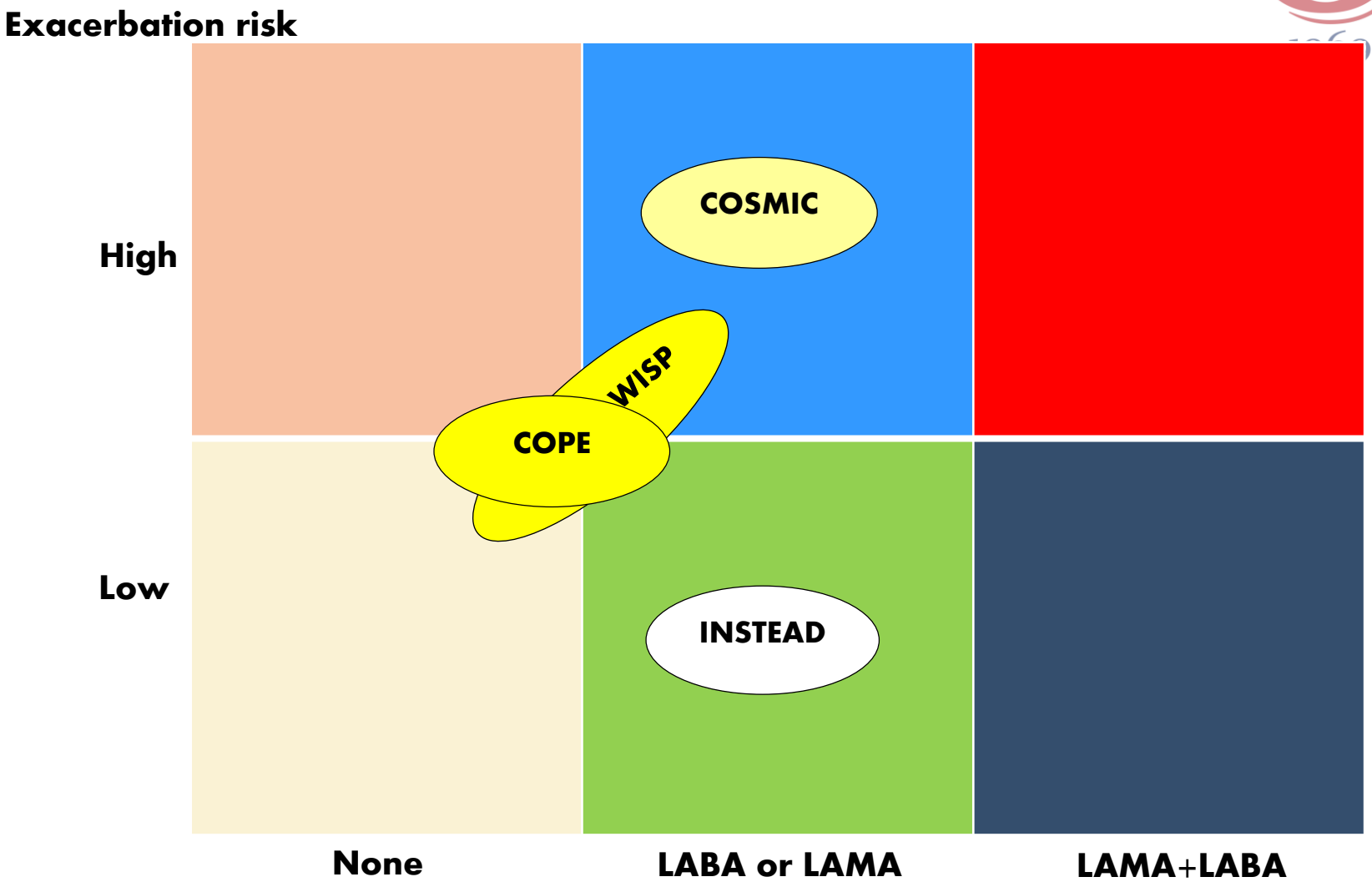


Trough FEV1 at 12wks



Exacerbation free at **26wks**

Withdrawn of ICS on exacerbations



Modified from IJCOPD 2018:13 2089–2099

WISDOM study

multinational, randomized, double-blind, parallel-group study

2485 COPD patients prescribed with SFC plus tiotropium for 6wks

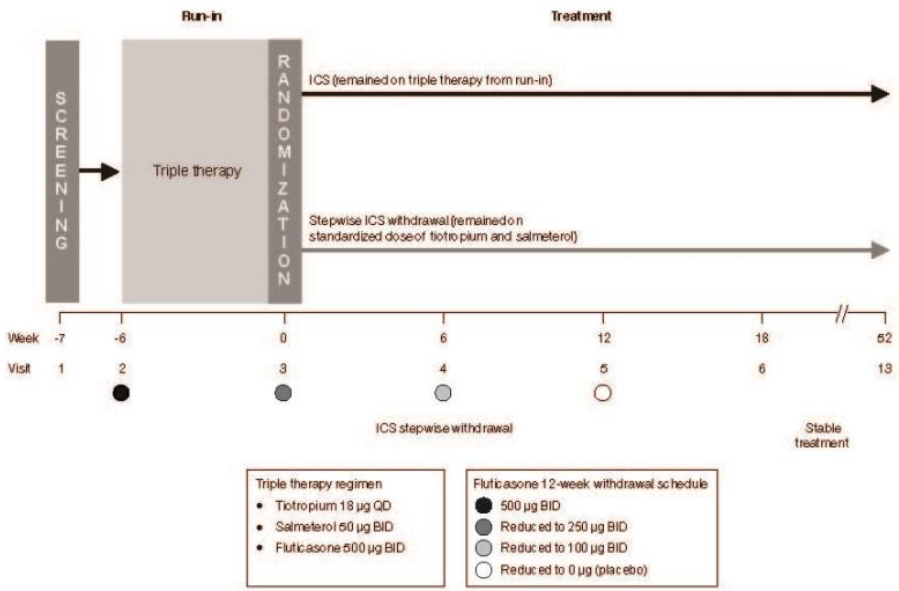
Patients: FEV1 <50%
≥1 COPD exacerbation history
Triple therapy in 39%

Flucicasone 500ug bid

52 wks

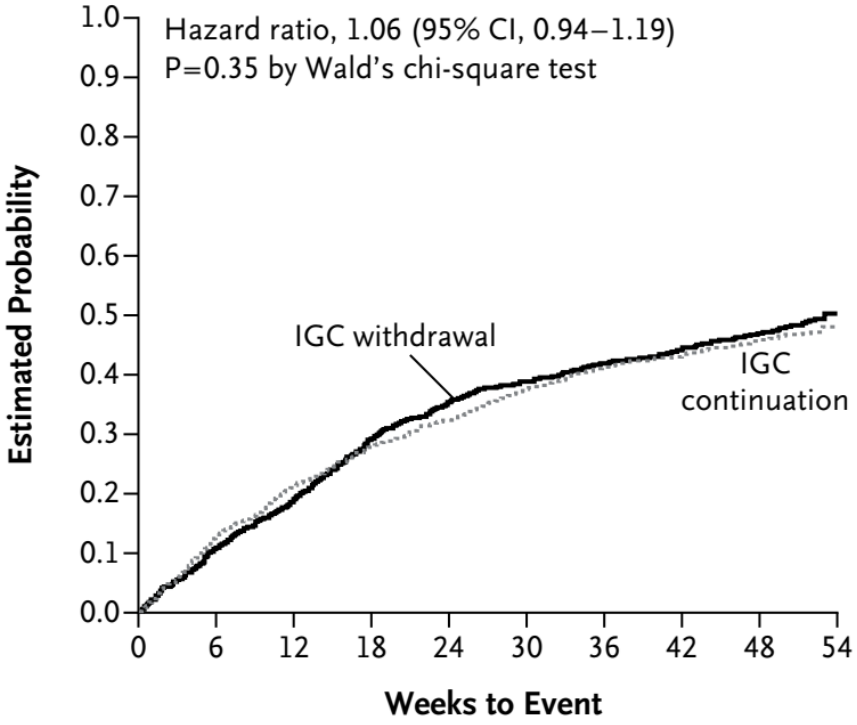
ICS withdrawn

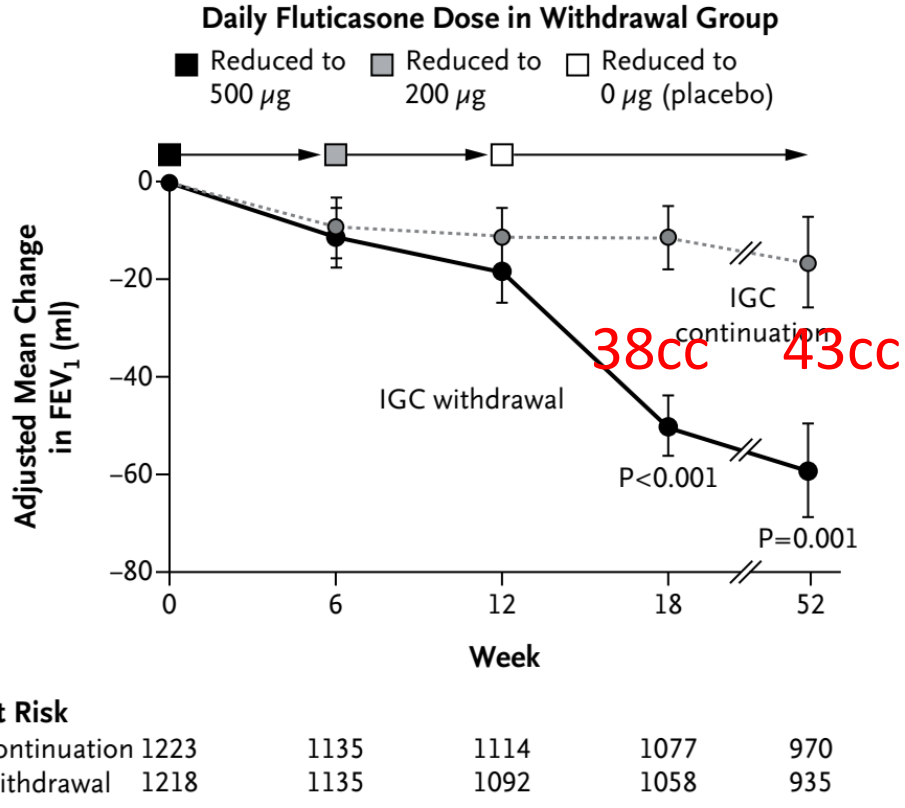
Non-inferiority on rate of exacerbation



N Engl J Med 2014;371:1285-94

No difference for AE but increased FEV1 decline

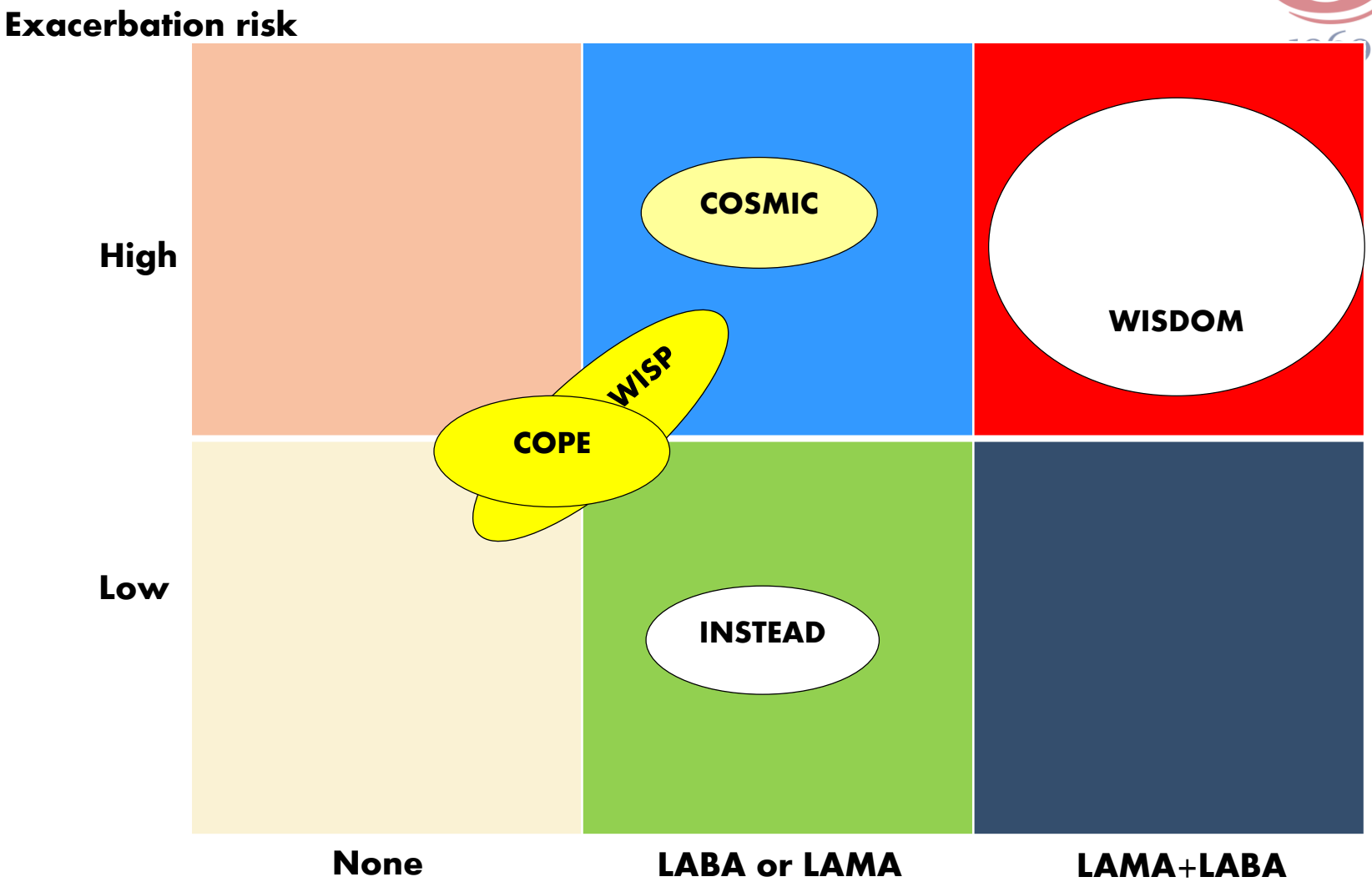




No. at Risk

IGC continuation	1223	1135	1114	1077	970
IGC withdrawal	1218	1135	1092	1058	935

Withdrawn of ICS on exacerbations



Modified from IJCOPD 2018:13 2089–2099

OPTIMO study

A prospective, multicenter, observation study (recruited from GP)

914 COPD patients prescribed with ICS + LABA for 12M

Patients: FEV1/VC<88%
FEV1>50%;
<2 exacerbations

ICS continued
n=539

6 months

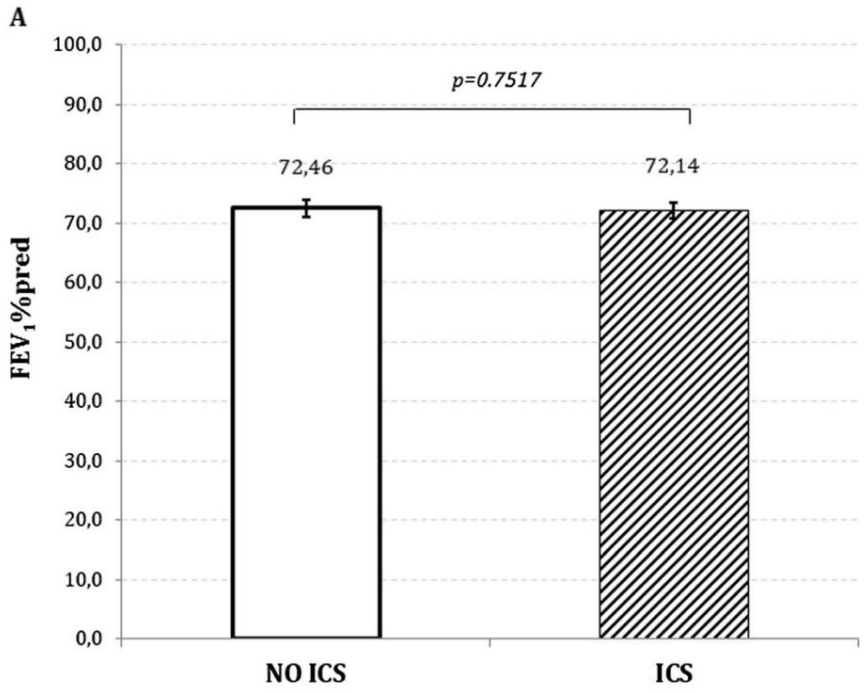
ICS withdrawn
N=374

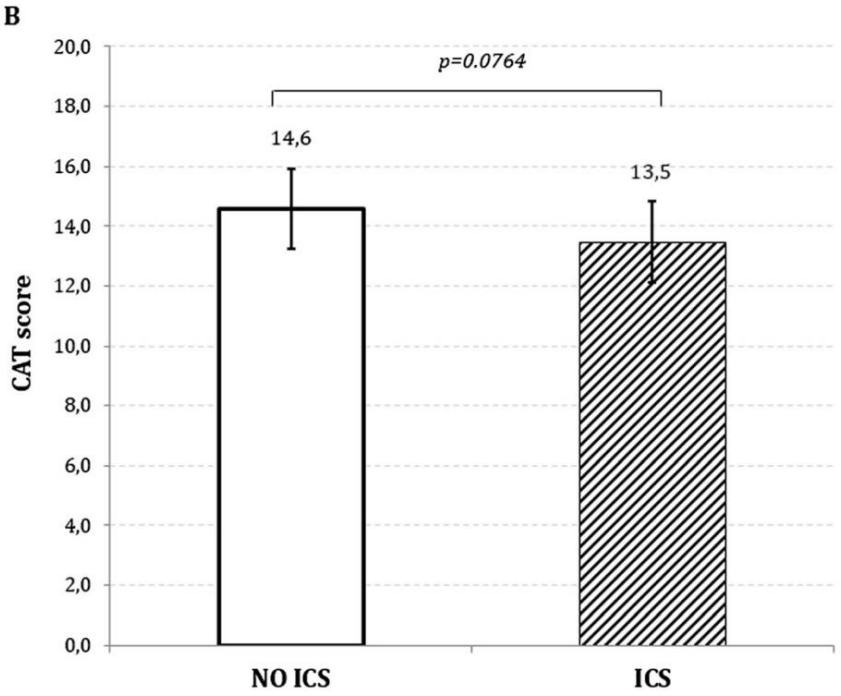
- TIOTROPIUM (27%)
- INDACATEROL (29%)
- FORMOTEROL/SALMETEROL (15%)
- TIOTROPIUM+INDACATEROL (20%)
- OTHER (9%)

FEV1,
CAT,
Exacerbations

Respiratory Research 2014, 15:77

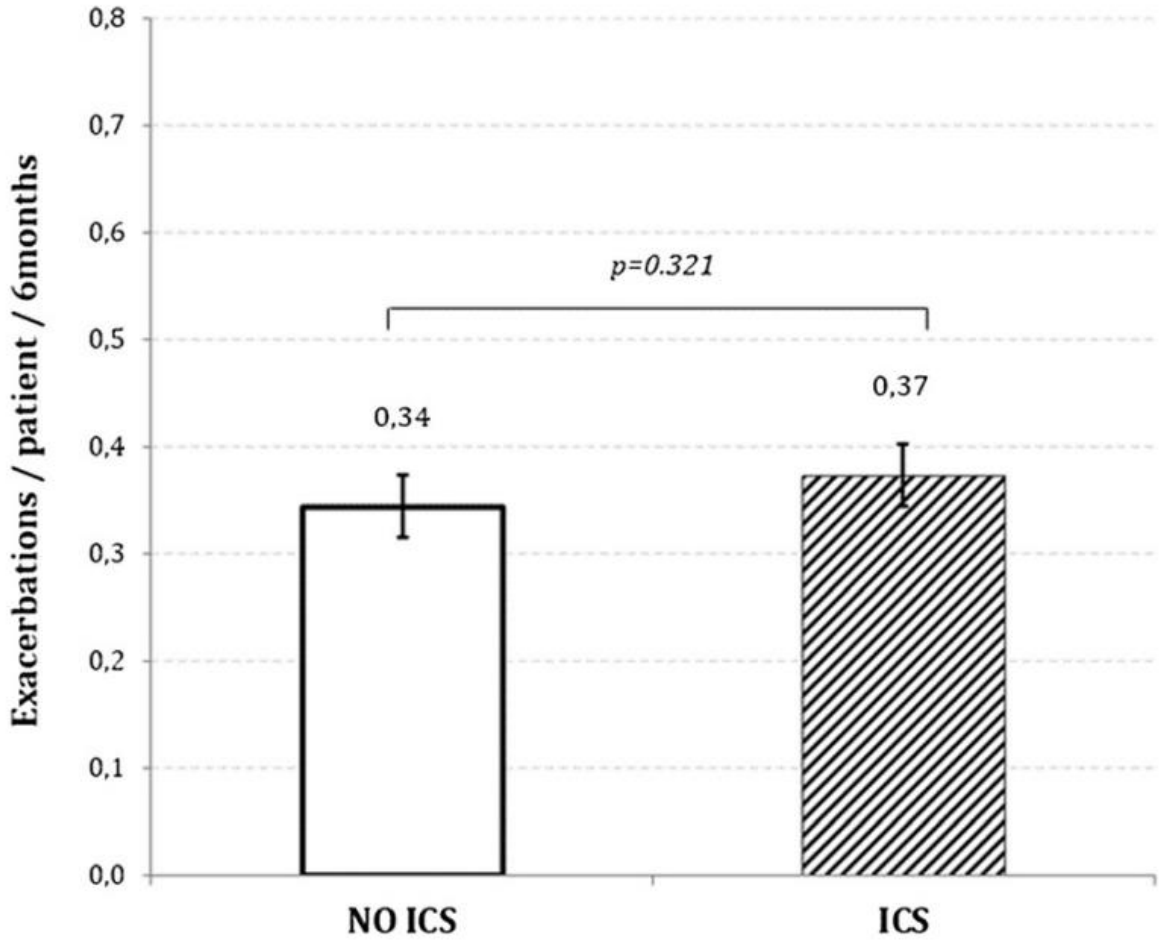
No FEV1 nor CAT difference



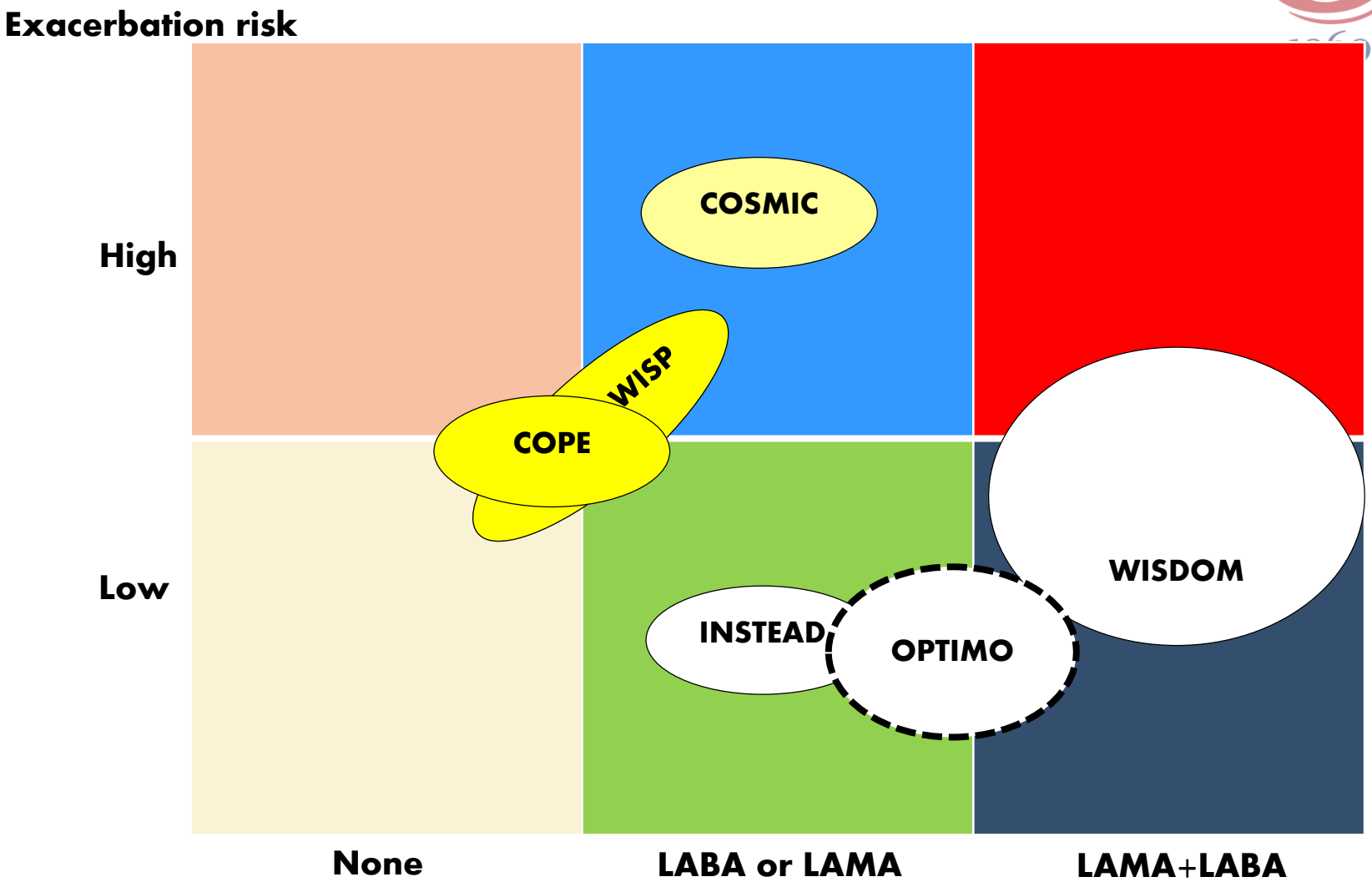


Respiratory Research 2014, 15:77

No difference for AE



Withdrawn of ICS on exacerbations



Modified from IJCOPD 2018:13 2089–2099

DACCORD study

An non-interventional, observational and prospective study

1365 COPD patients prescribed with ICS

Patients: diagnosed with COPD
>70% no AE in the past 6M

ICS continued
n=1022

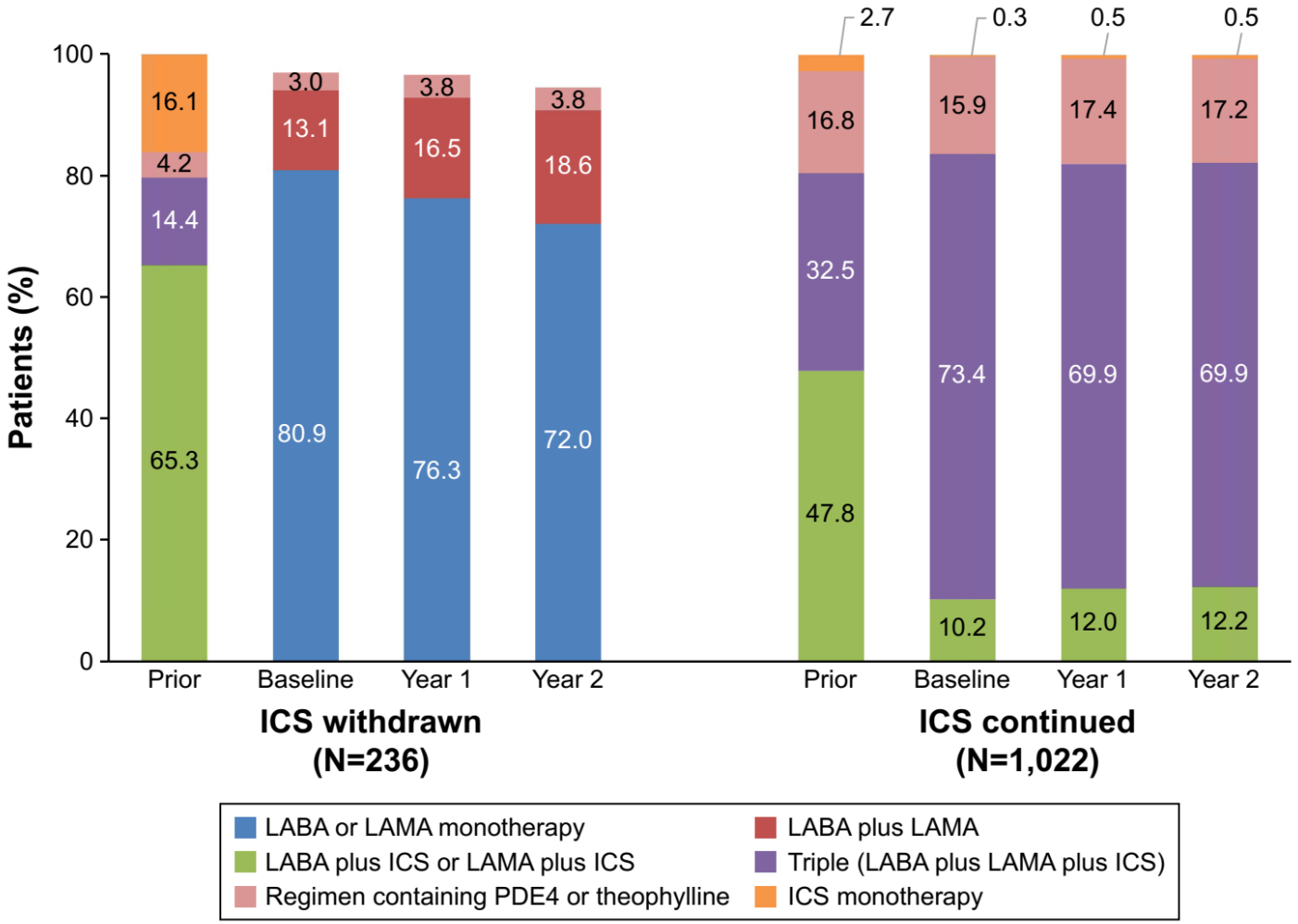
2 years

ICS withdrawn
N=236

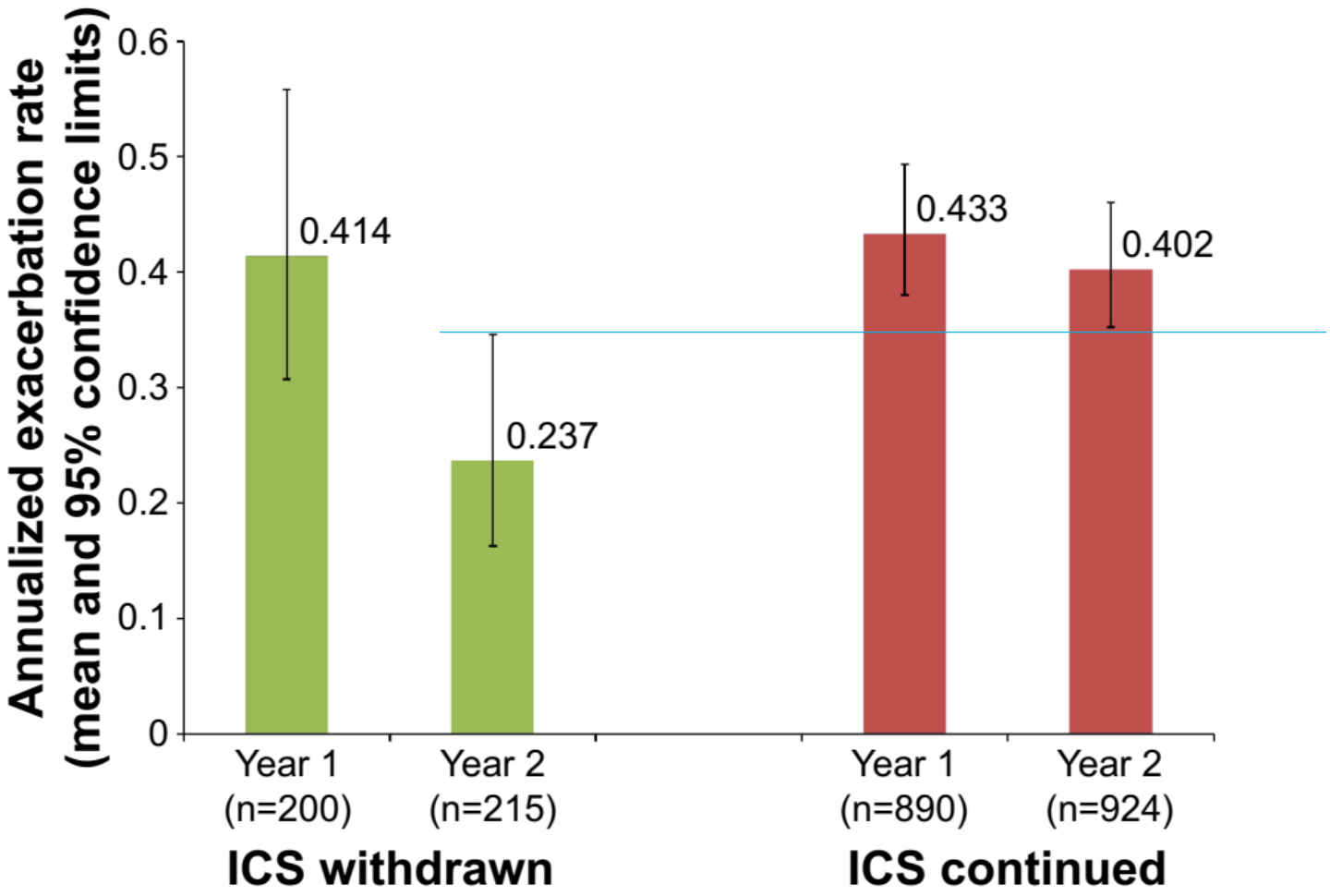
Exacerbation, health status

International Journal of COPD 2017:12 487–494

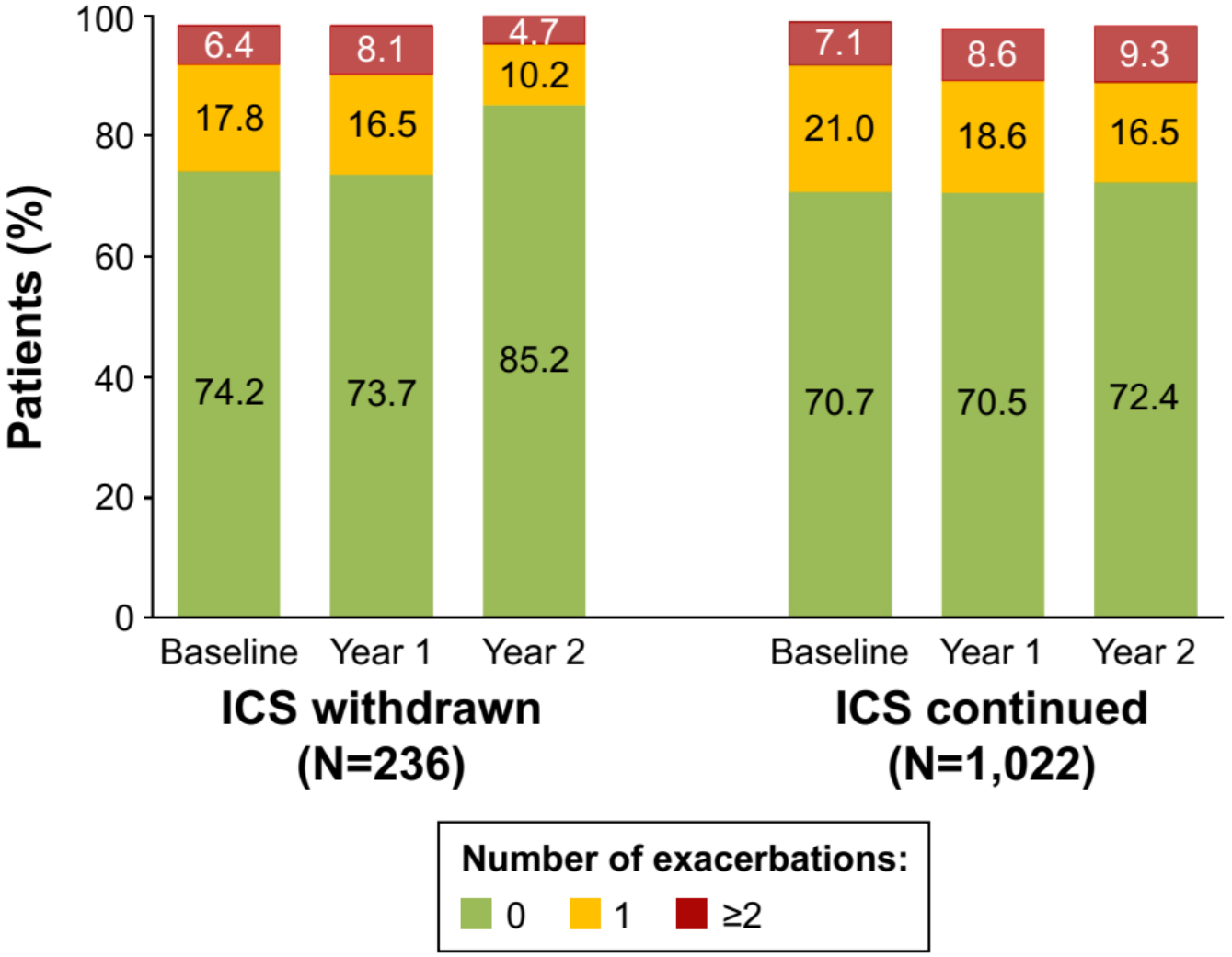
Regimen


Patients (%)
100
80
60
40
20
0
16.1
4.2
14.4
65.3
3.0
13.1
80.9
3.8
16.5
76.3
3.8
18.6
72.0
2.7
16.8
32.5
47.8
0.3
15.9
73.4
10.2
0.5
17.4
69.9
12.0
0.5
17.2
69.9
12.2
Prior
Baseline
Year 1
Year 2
Prior
Baseline
Year 1
Year 2
ICS withdrawn
(N=236)
ICS continued
(N=1,022)
LABA or LAMA monotherapy
LABA plus LAMA
LABA plus ICS or LAMA plus ICS
Triple (LABA plus LAMA plus ICS)
Regimen containing PDE4 or theophylline
ICS monotherapy

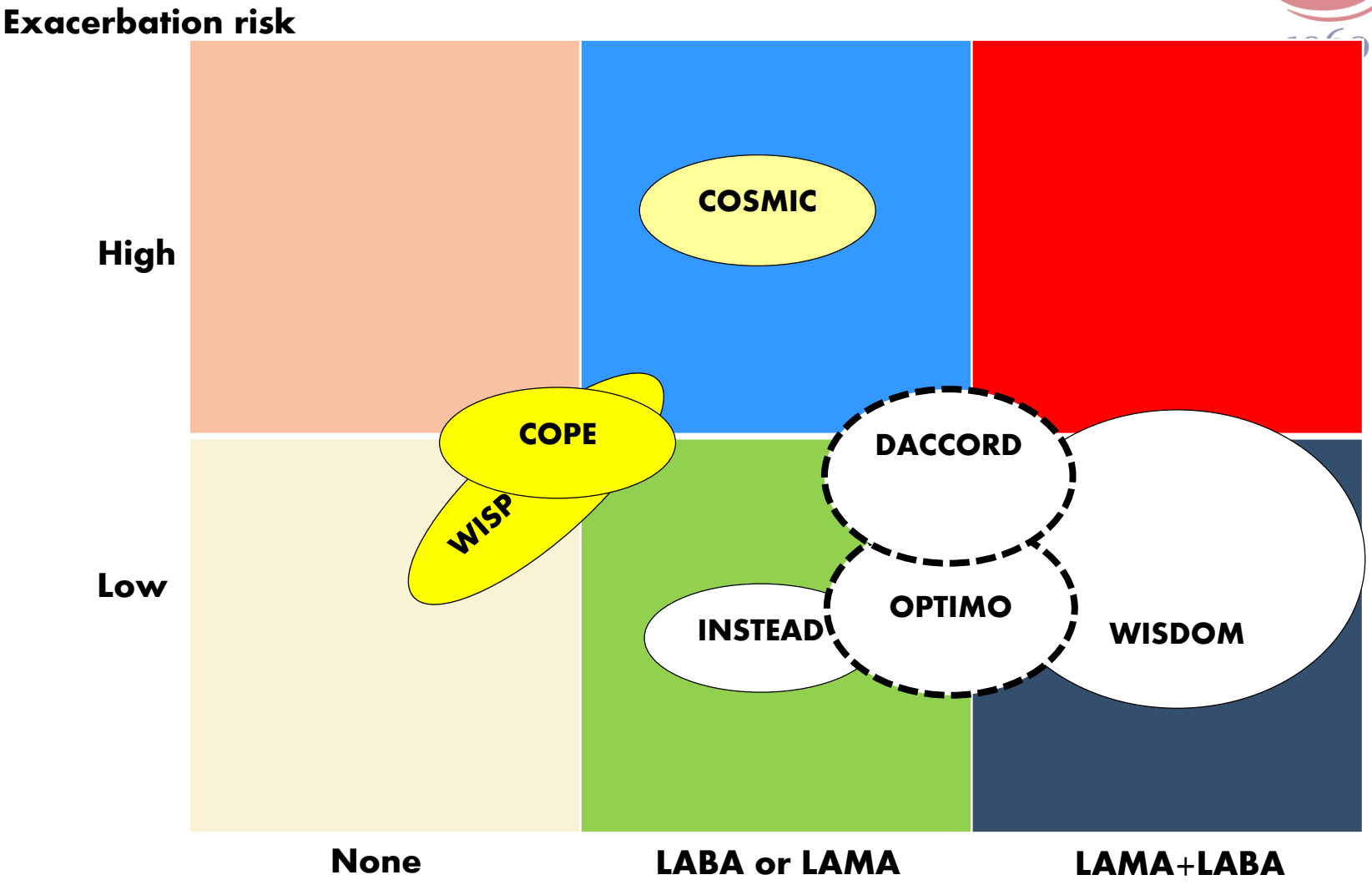
Annual Exacerbation rate



More Nonexacerbators in ICS-Withdrawn Group at Year 2

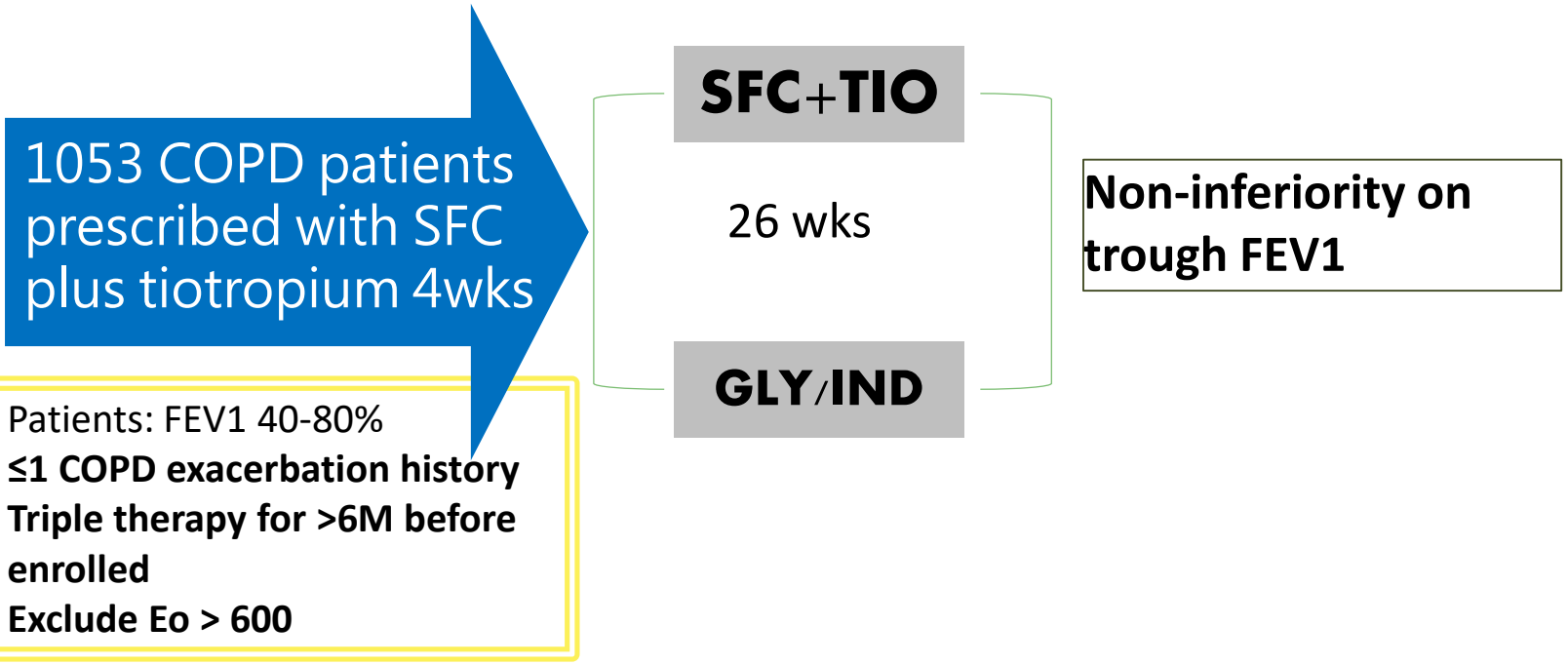


Withdrawn of ICS on exacerbations



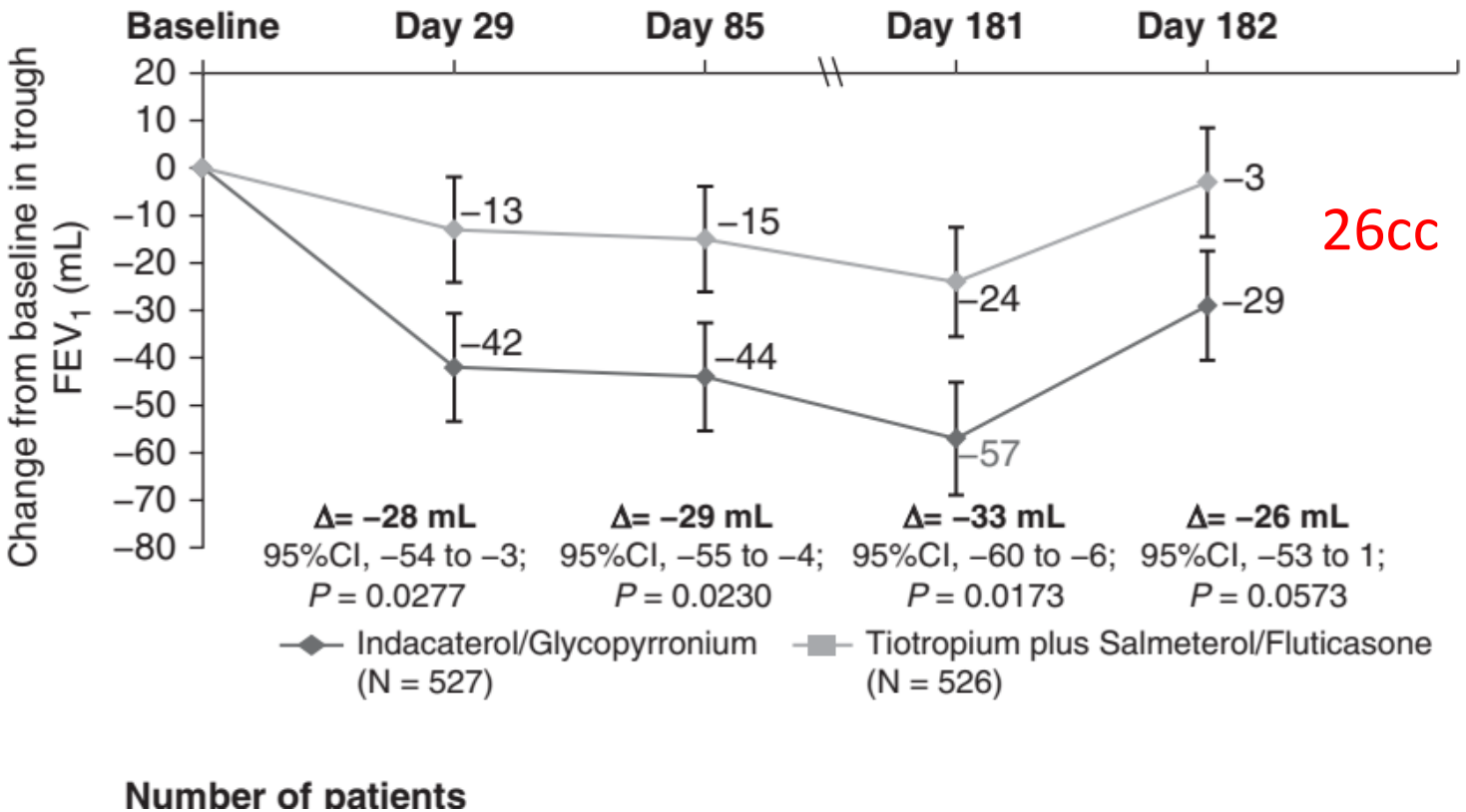
International Journal of COPD 2018:13 2089–2099

SUNSET study:
Double blind, triple dummy



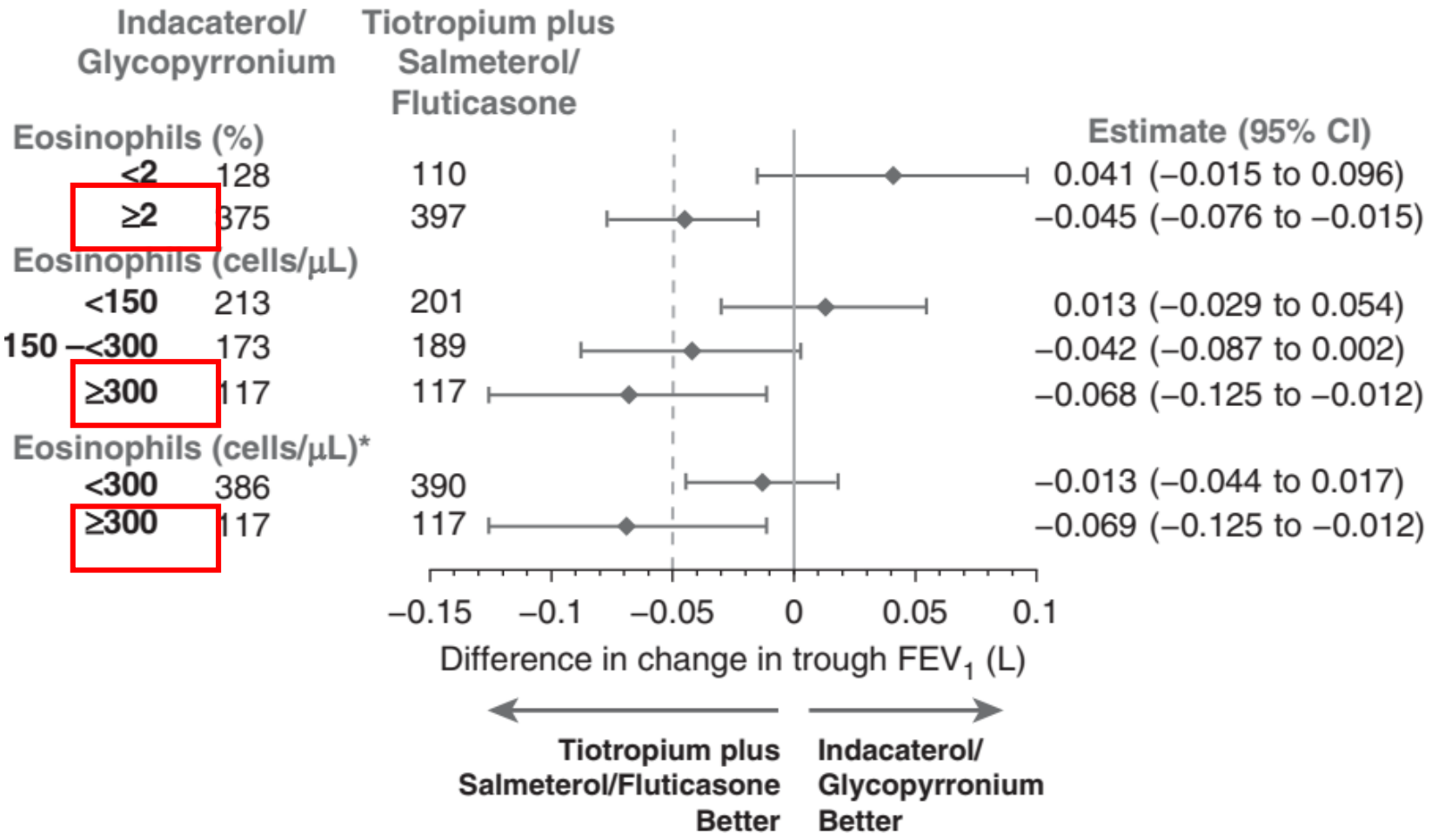
AJRCCM 2018;198;3,329–339

FEV1 decline was inferior in ICS withdrawn patients

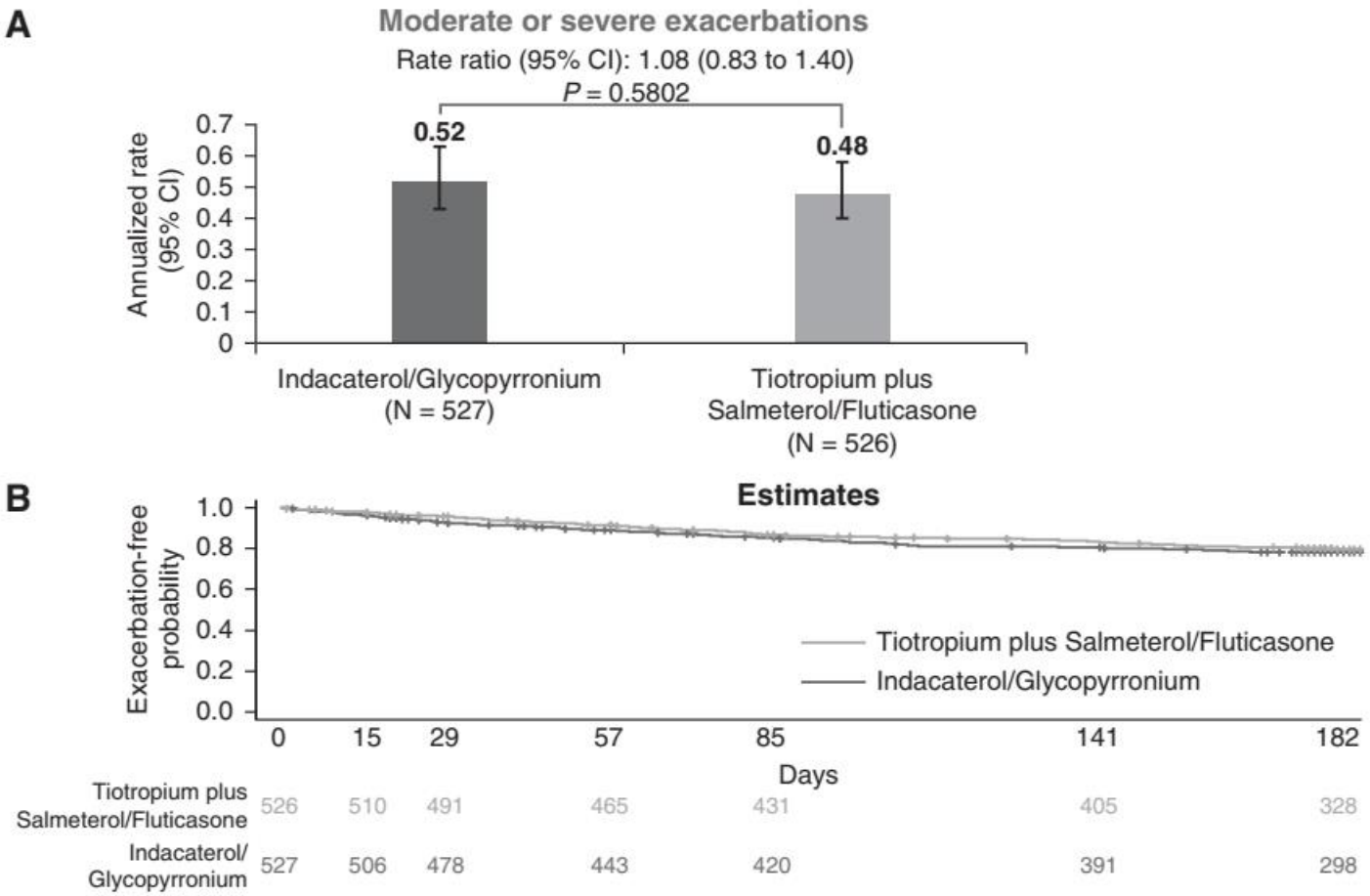


26cc

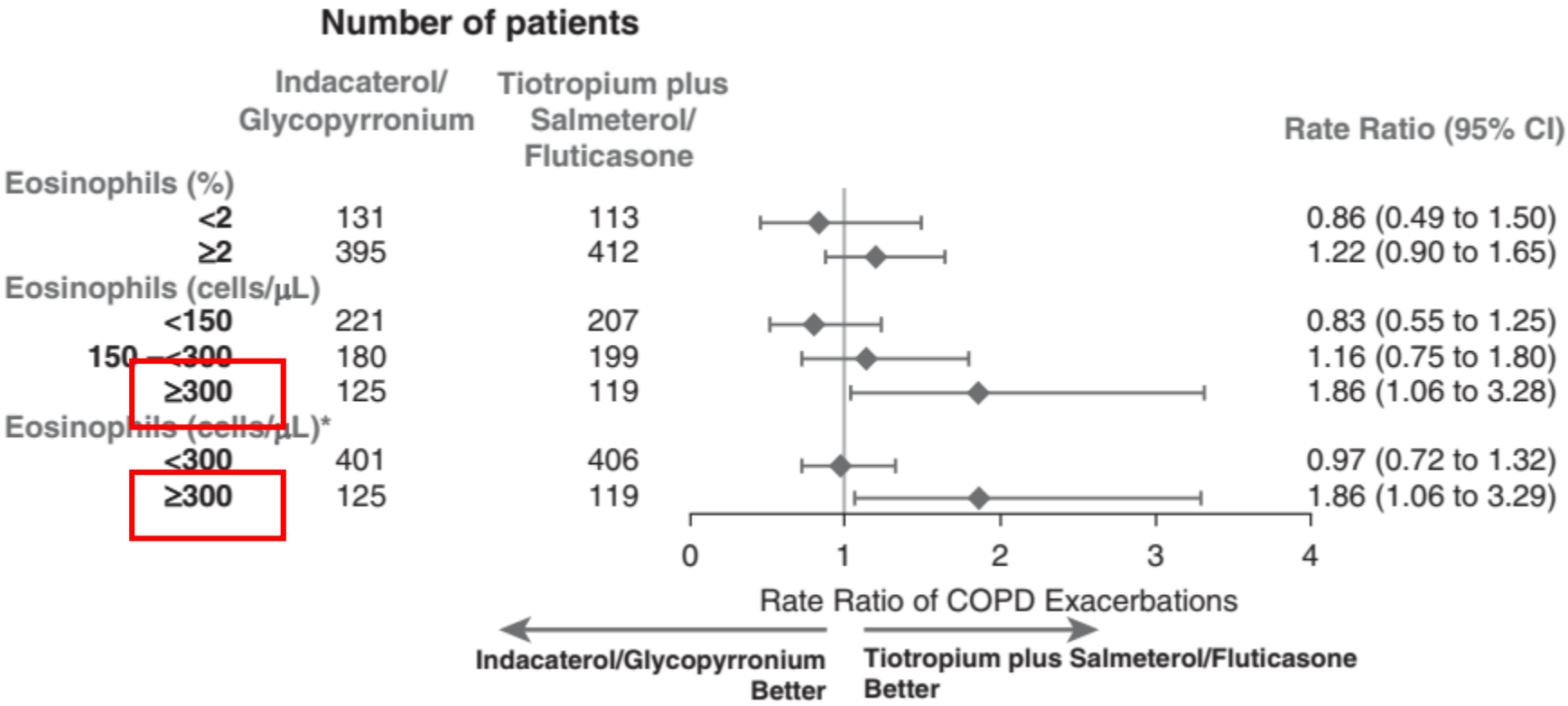
The difference was noted in patient with Eo >2% or 300/cumm



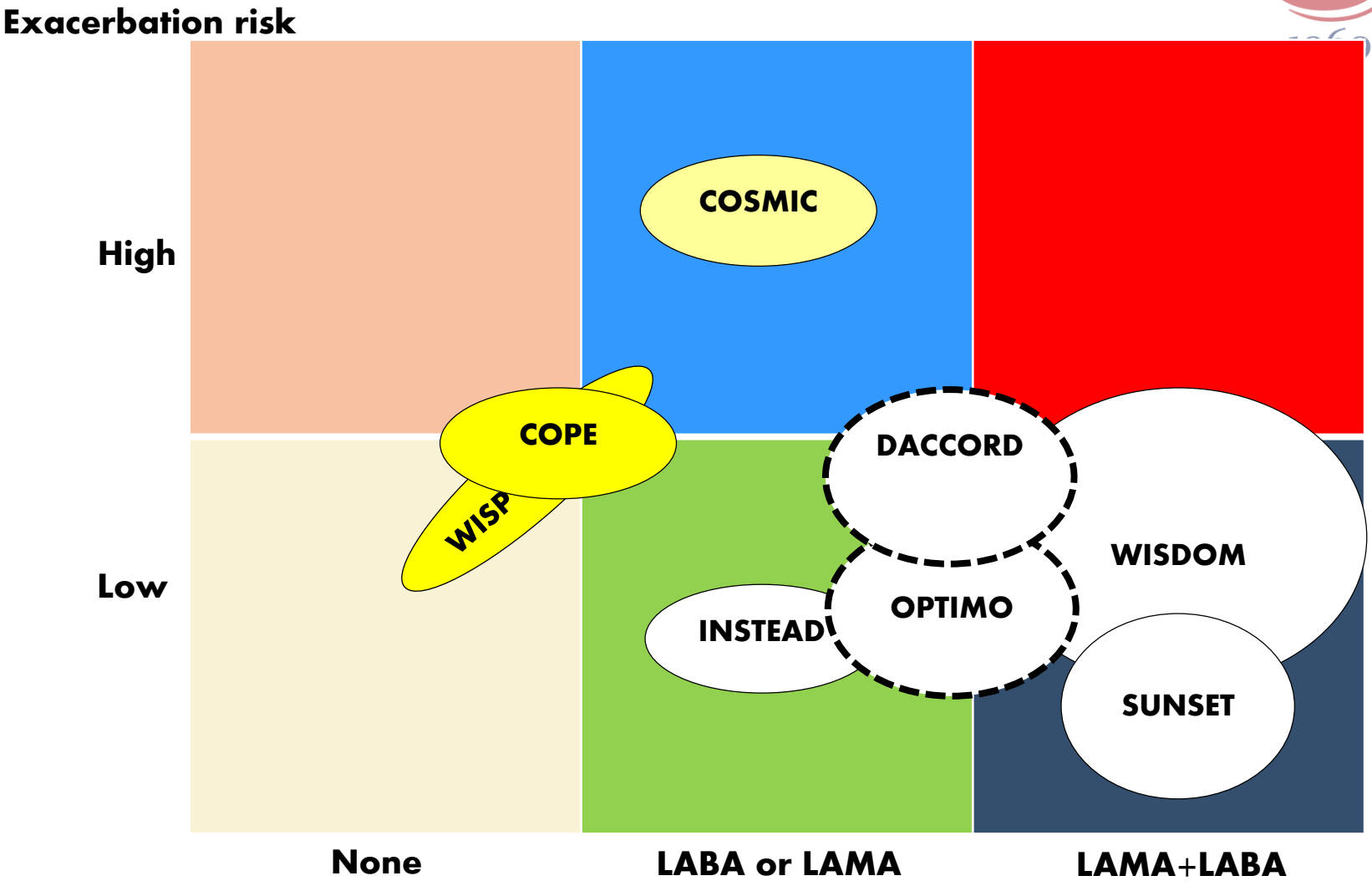
No Exacerbation difference



More AE in patients with Eo>300/cumm



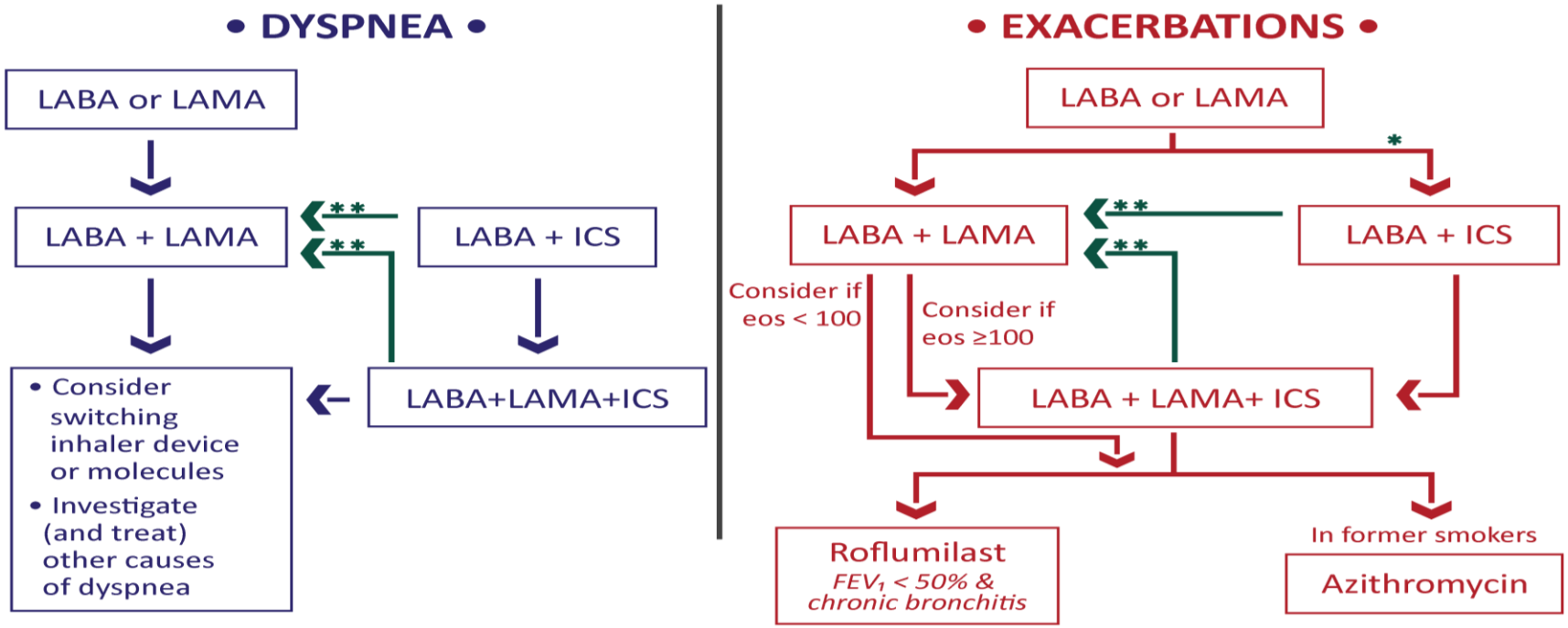
Withdrawn of ICS on exacerbations



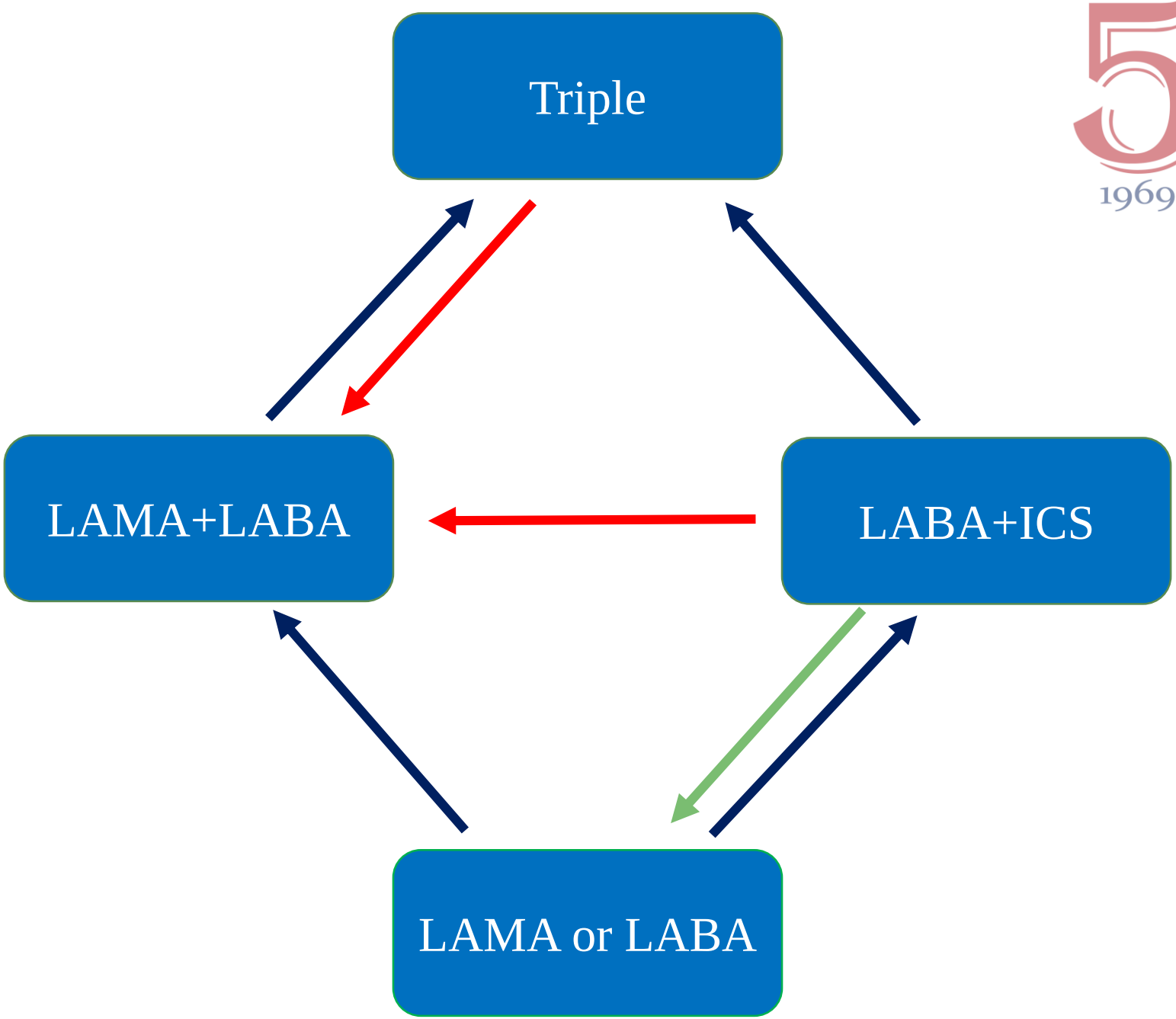
International Journal of COPD 2018:13 2089–2099

Follow-up Treatment

1. **IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.**
2. **IF NOT:**
   - ✓ Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - ✓ Place patient in box corresponding to current treatment & follow indications
   - ✓ Assess response, adjust and review
   - ✓ These recommendations do not depend on the ABCD assessment at diagnosis



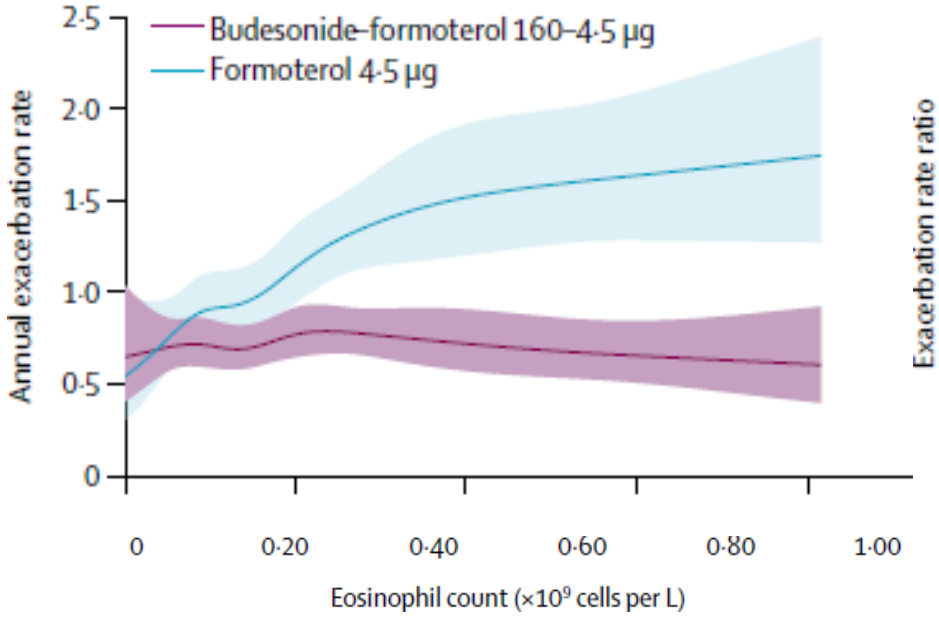
eos = blood eosinophil count (cells/µL)
** Consider if eos ≥ 300 or eos ≥ 100 AND ≥2 moderate exacerbations / 1 hospitalization*
*** Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS*

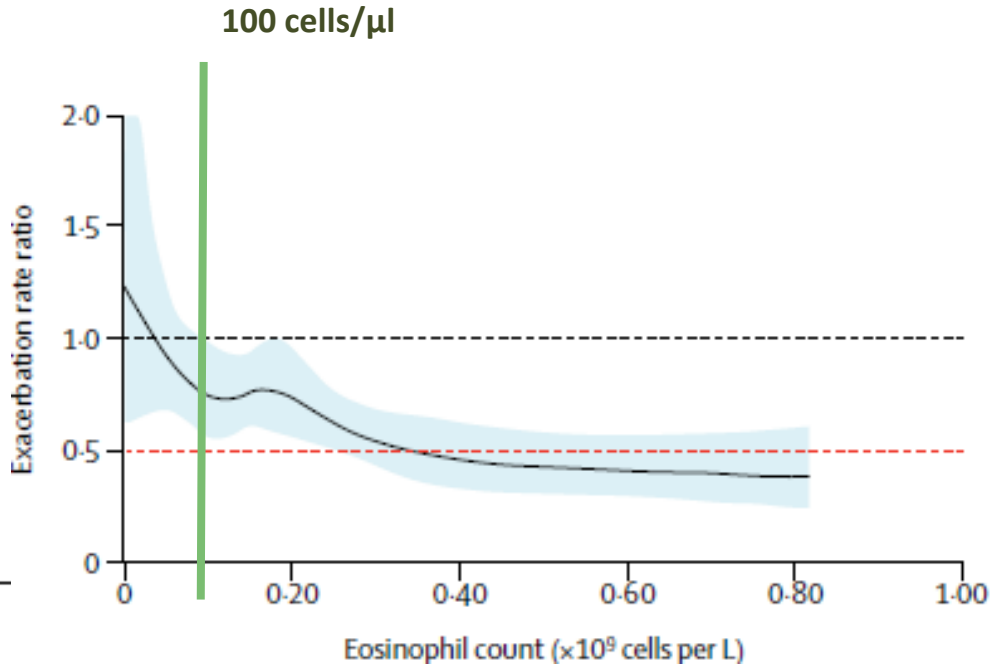

Triple
LAMA+LABA
LABA+ICS
LAMA or LABA

Conclusions

- ICS do better than prn short acting bronchodilators
- Long acting bronchodilators prevent exacerbation better than ICS in **low exacerbation risk** patients
- The run-in periods are between 3~12M
- Sudden withdrawal of ICS is acceptable in most clinical practice and practicable in real world
- ICS withdrawal leads to a drop of FEV1 ~30-50 ml/yr

ICS has treatment effects in high Eosinophil COPD



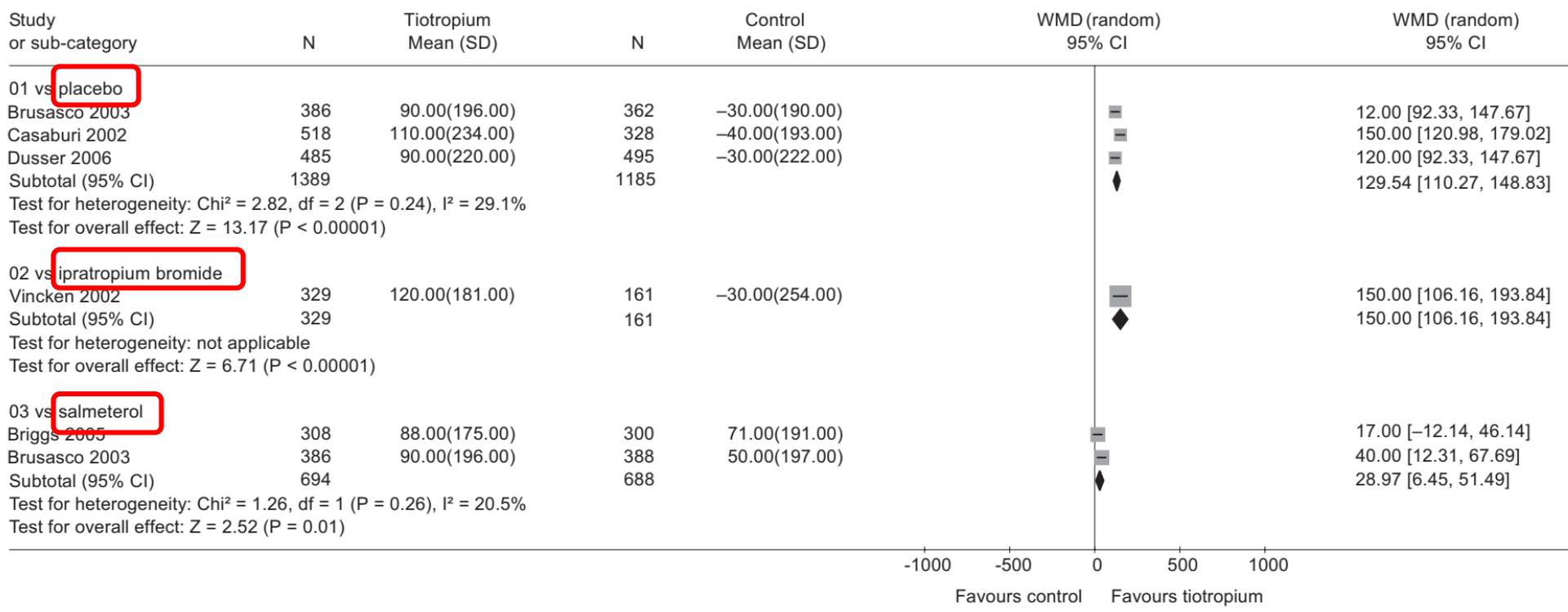


Lancet Respir Med. 2018 Feb;6(2):117-126

- 1. ICS tapering
- 2. Dual therapy → monotherapy
- 3. Triple therapy → combination therapy

LAMA (tiotropium) for stable COPD

Changes in trough FEV1



Thorax 2006;61:854–862

Respir Care 2011;56(4):477–487

LAMA (tiotropium) for stable COPD

A

Exacerbation

Author, Year	Tiotropium (*n*/*N*)	Placebo (*n*/*N*)	OR (95% CI) Random	Weight %*
Brusasco[21] 2003	129//402	156/400	0.74 (0.55–0.99)	10.85
Casaburi[19] 2002	198/550	156/371	0.78 (0.59–1.02)	11.69
Chan[27] 2007	268/608	125/305	1.14 (0.86–1.50)	11.31
Dusser[25] 2006	248/497	305/506	0.66 (0.51–0.84)	12.55
Freeman[28] 2007	19/200	35/195	0.48 (0.26–0.87)	4.00
Johansson[29] 2008	2/107	4/117	0.54 (0.10–3.00)	0.57
Moita[30] 2008	6/147	6/164	1.12 (0.35–3.55)	1.23
Niewoehner[24] 2005	255/914	296/915	0.81 (0.66–0.99)	15.00
Tashkin[14] 2008	2001/2986	2049/3006	0.95 (0.85–1.06)	19.90
Tonnel[31] 2008	101/266	130/288	0.74 (0.53–1.04)	9.09
Voshaar[33] 2008	26/180	21/181	1.29 (0.69–2.38)	3.80
Subtotal (95% CI)	6857	6267	0.83 (0.72–0.94)	100

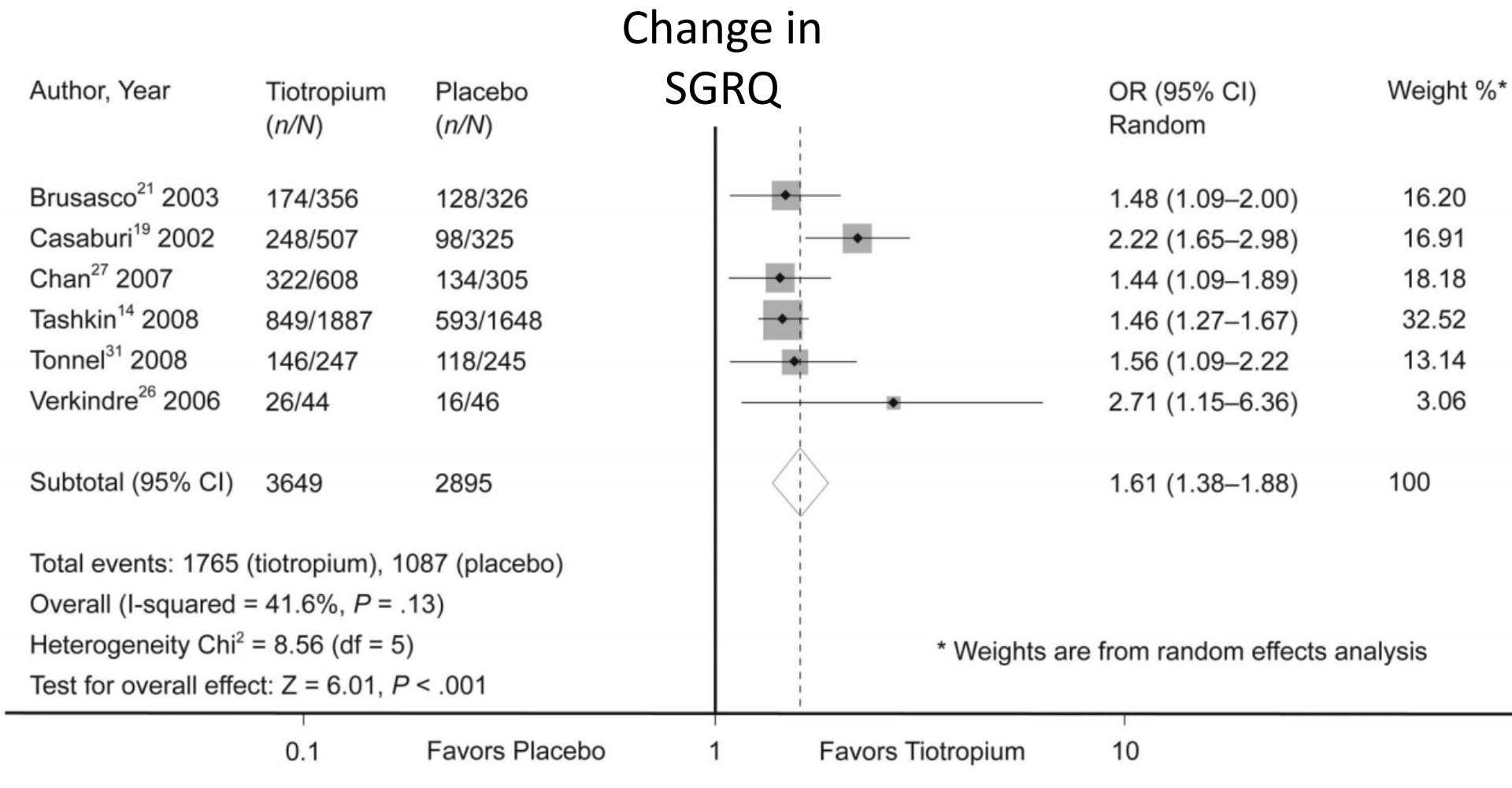
Total events: 3253 (tiotropium), 3283 (placebo)
Overall (I-squared = 49.7%, $P = .03$)
Heterogeneity Chi^2 = 19.89 (df = 10)
Test for overall effect: Z = 2.86, $P < .004$

* Weights are from random effects analysis

0.1 Favors Placebo 1 Favors Tiotropium 10

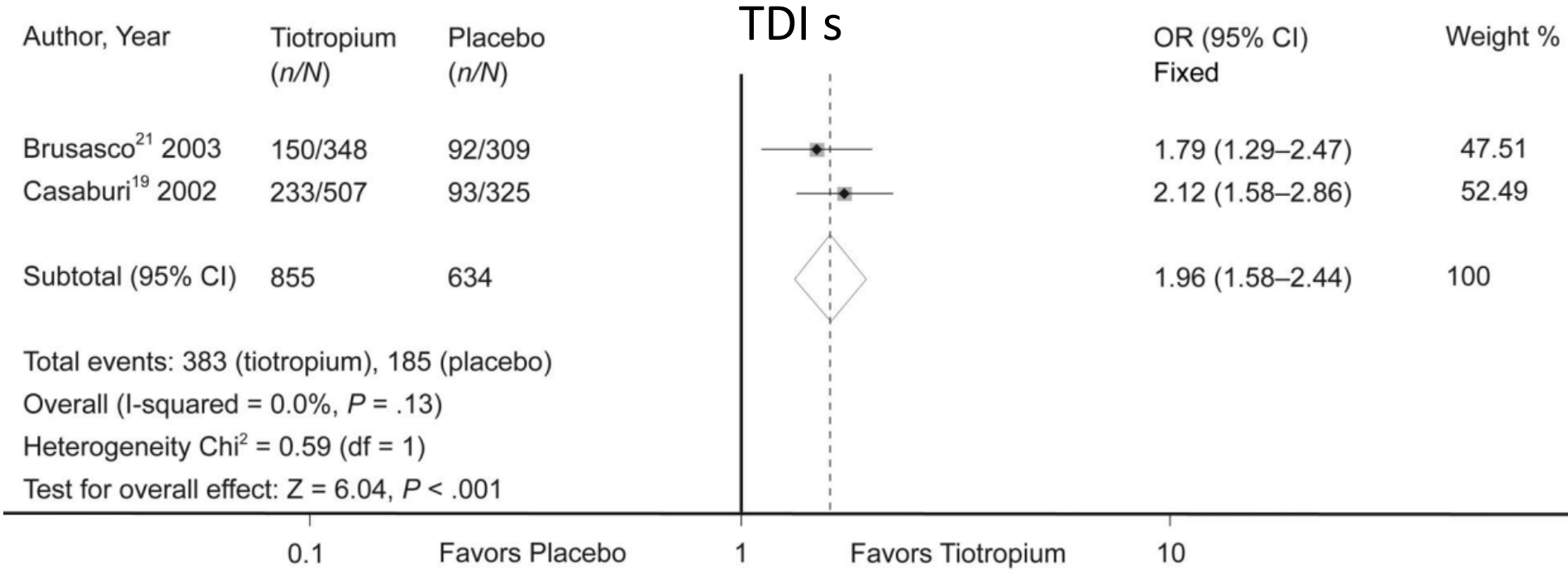
Respir Care 2011;56(4):477–487

LAMA (tiotropium) for stable COPD

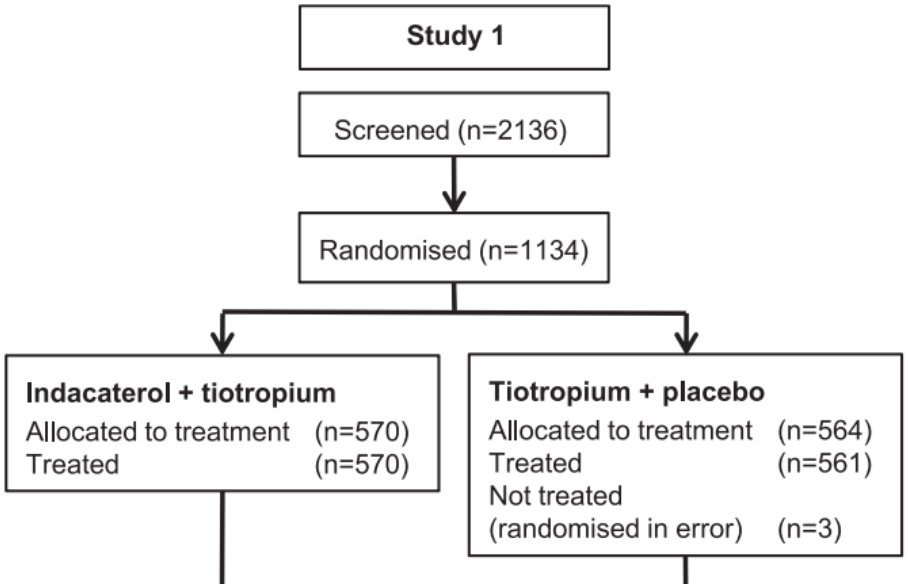


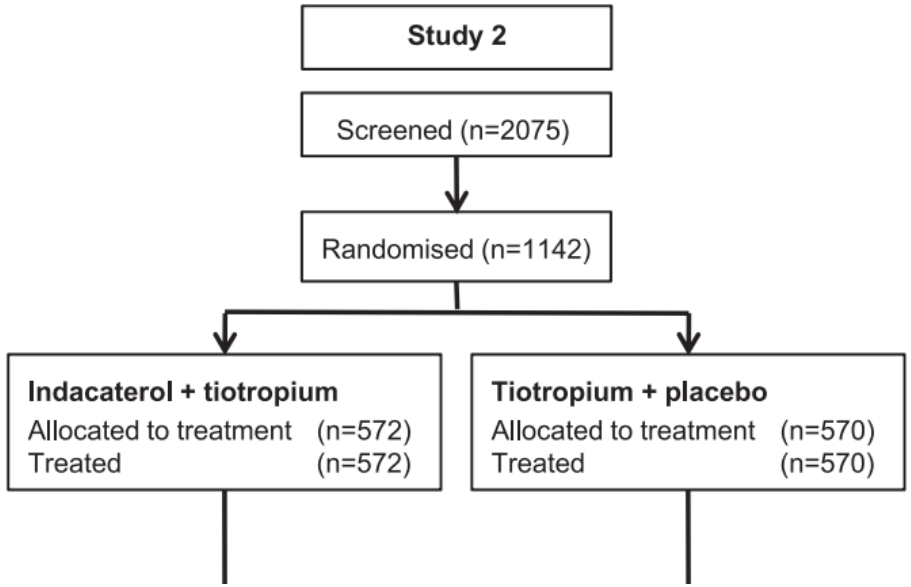
Respir Care 2011;56(4):477–487

LAMA (tiotropium) for stable COPD



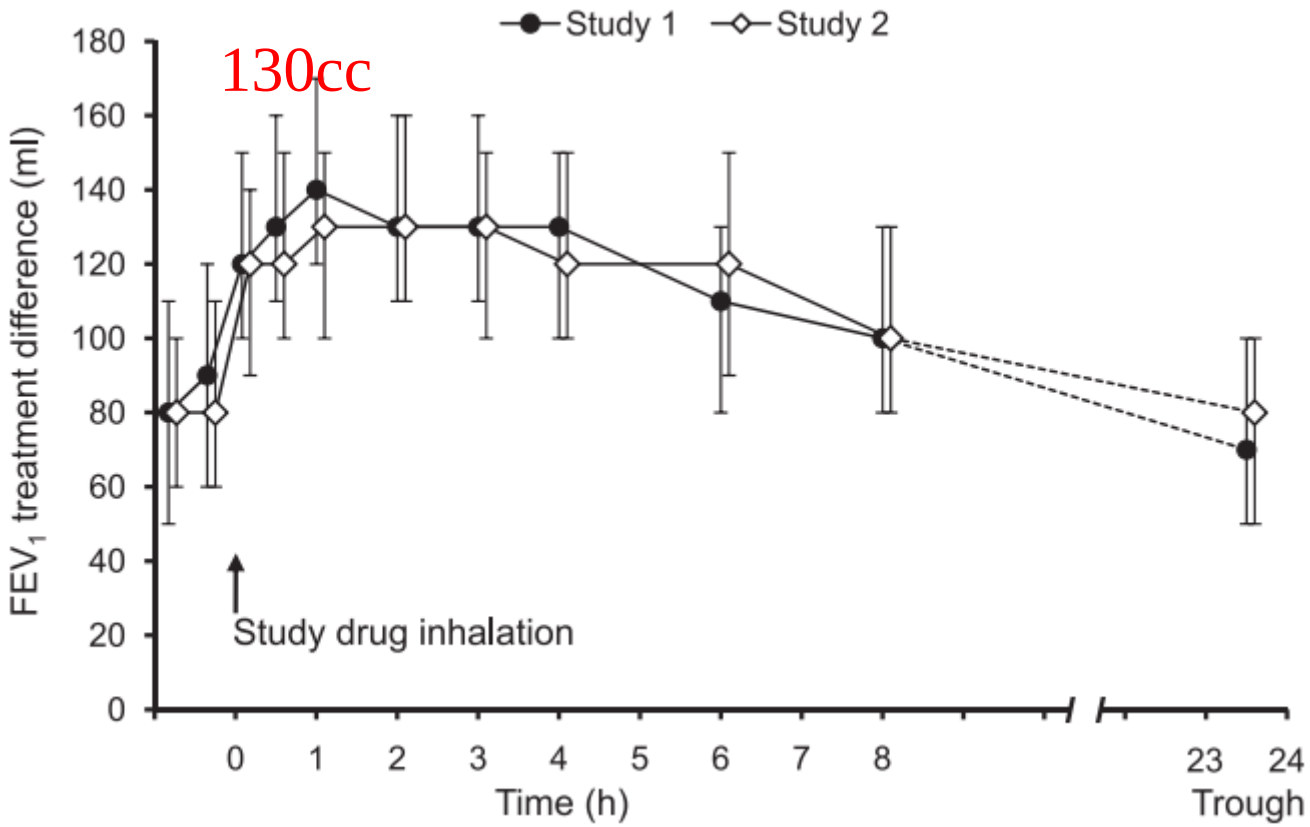
Indacaterol+ tiotropium in severe GOLD II & III COPD





INTRUST Thorax 2012;67:781-788

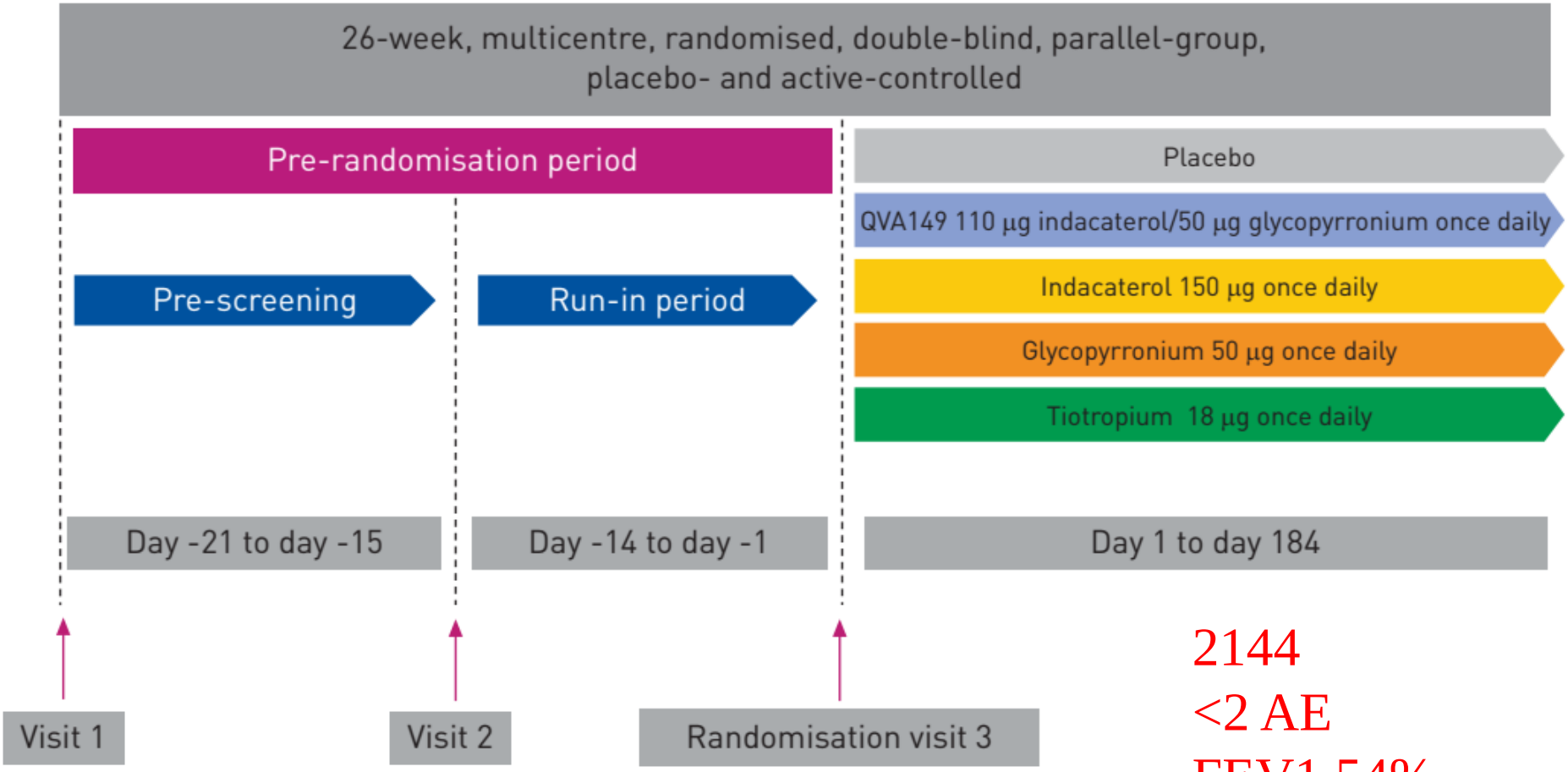
FEV1 difference



Thorax 2012;67:781-788

Eur Respir J 2013; 42: 1484–1494

Shine study

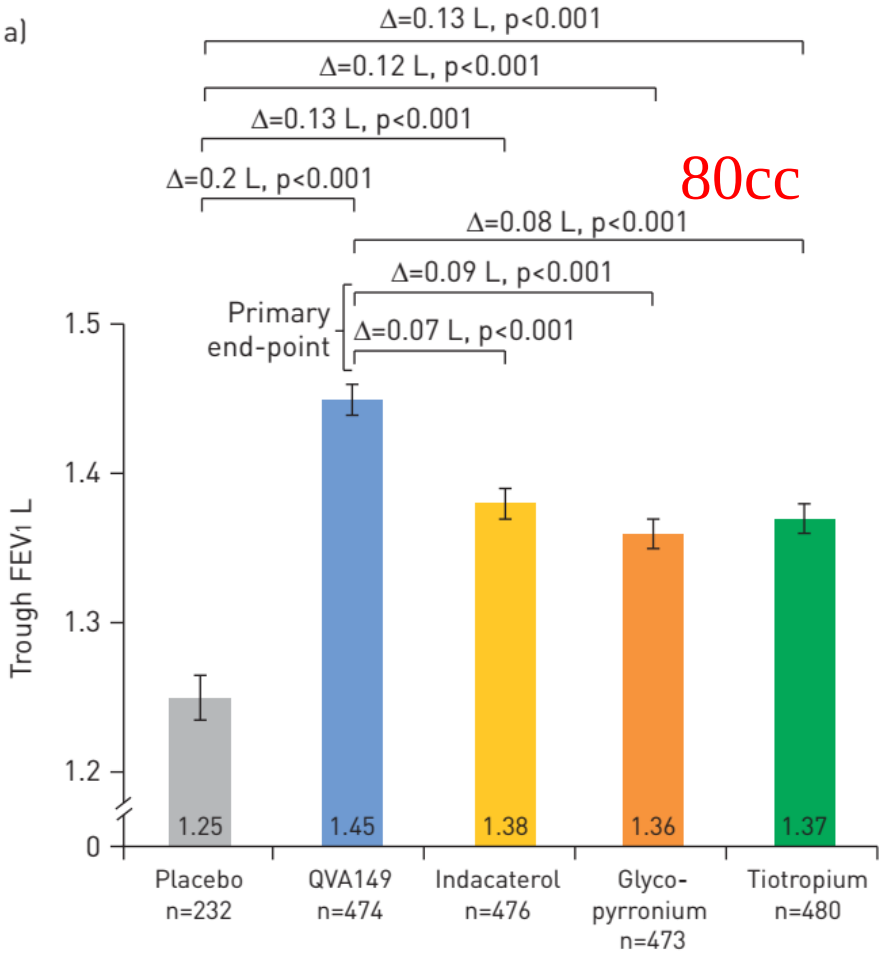


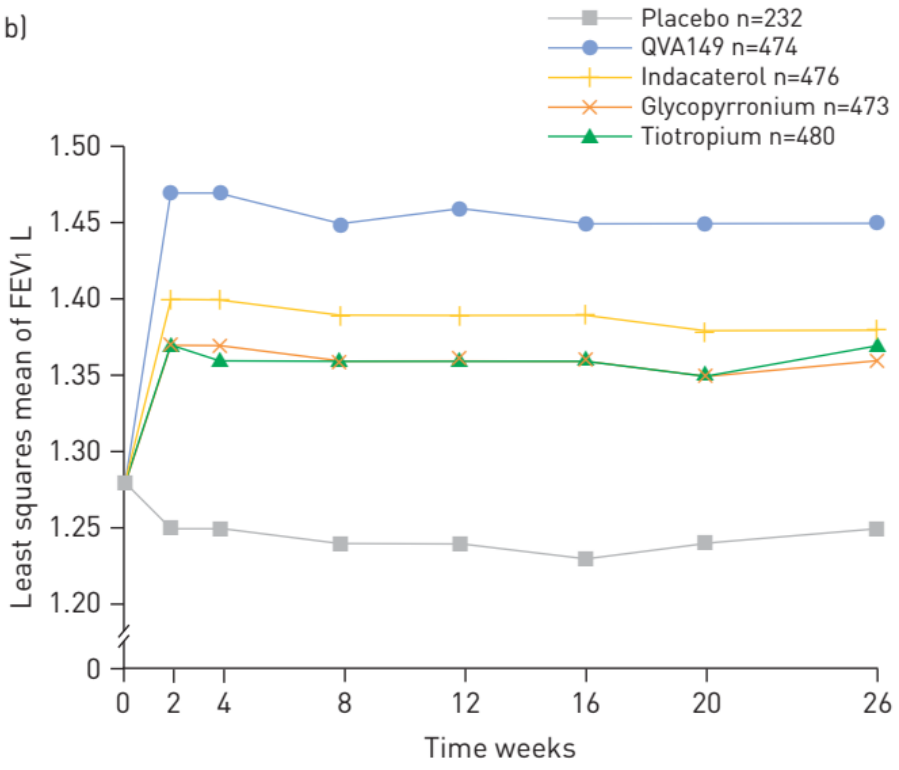
2144
<2 AE
FEV1 54%

Eur Respir J 2013; 42: 1484–1494

FEV1 improved more with dual bronchodilator

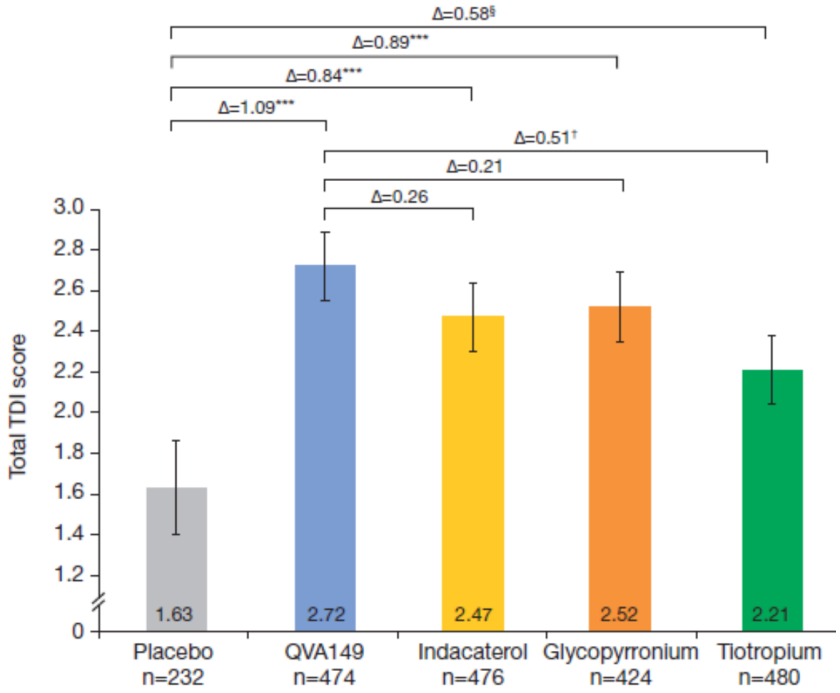
80cc

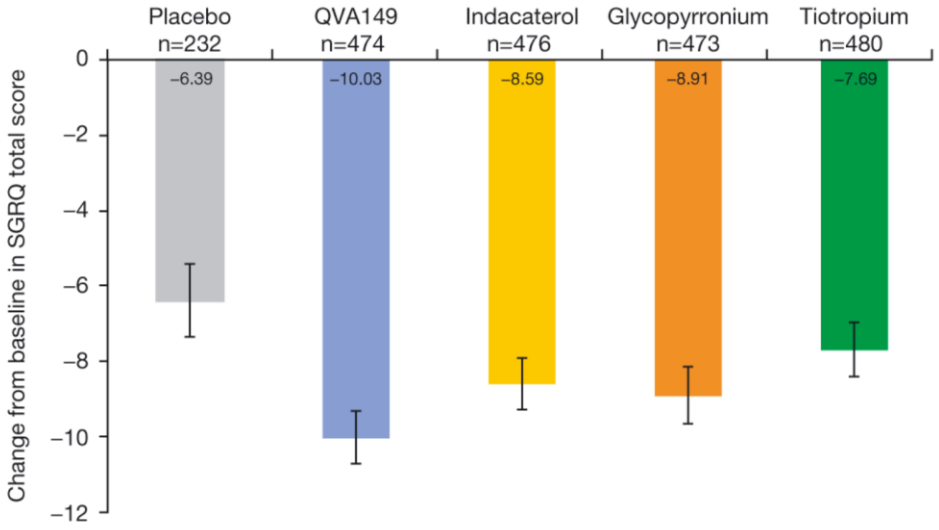




Eur Respir J 2013; 42: 1484–1494

More improved dyspnea and quality of life

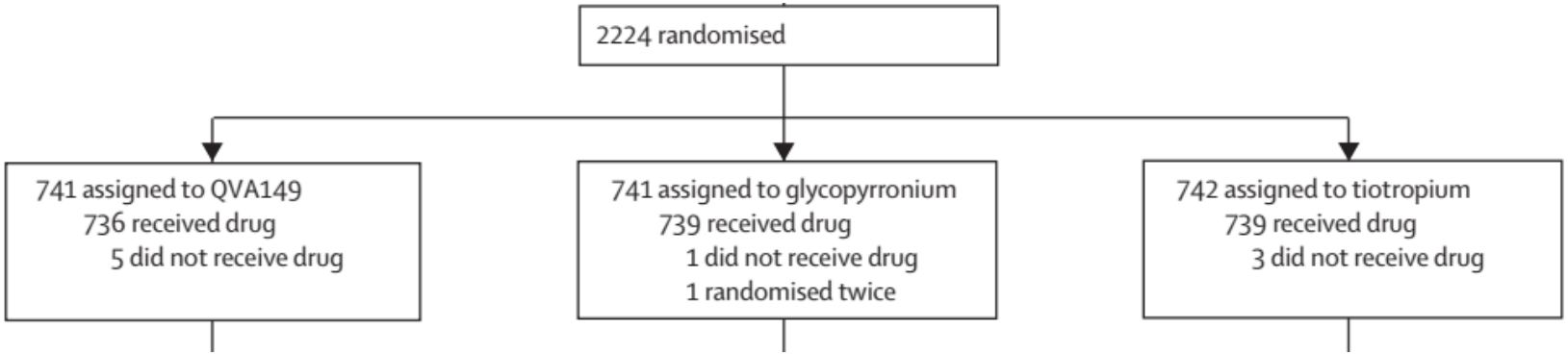




Lancet Respir Med 2013;1: 199–209

Spark study

- COPD FEV1 < 50%
- >1AE in the past year

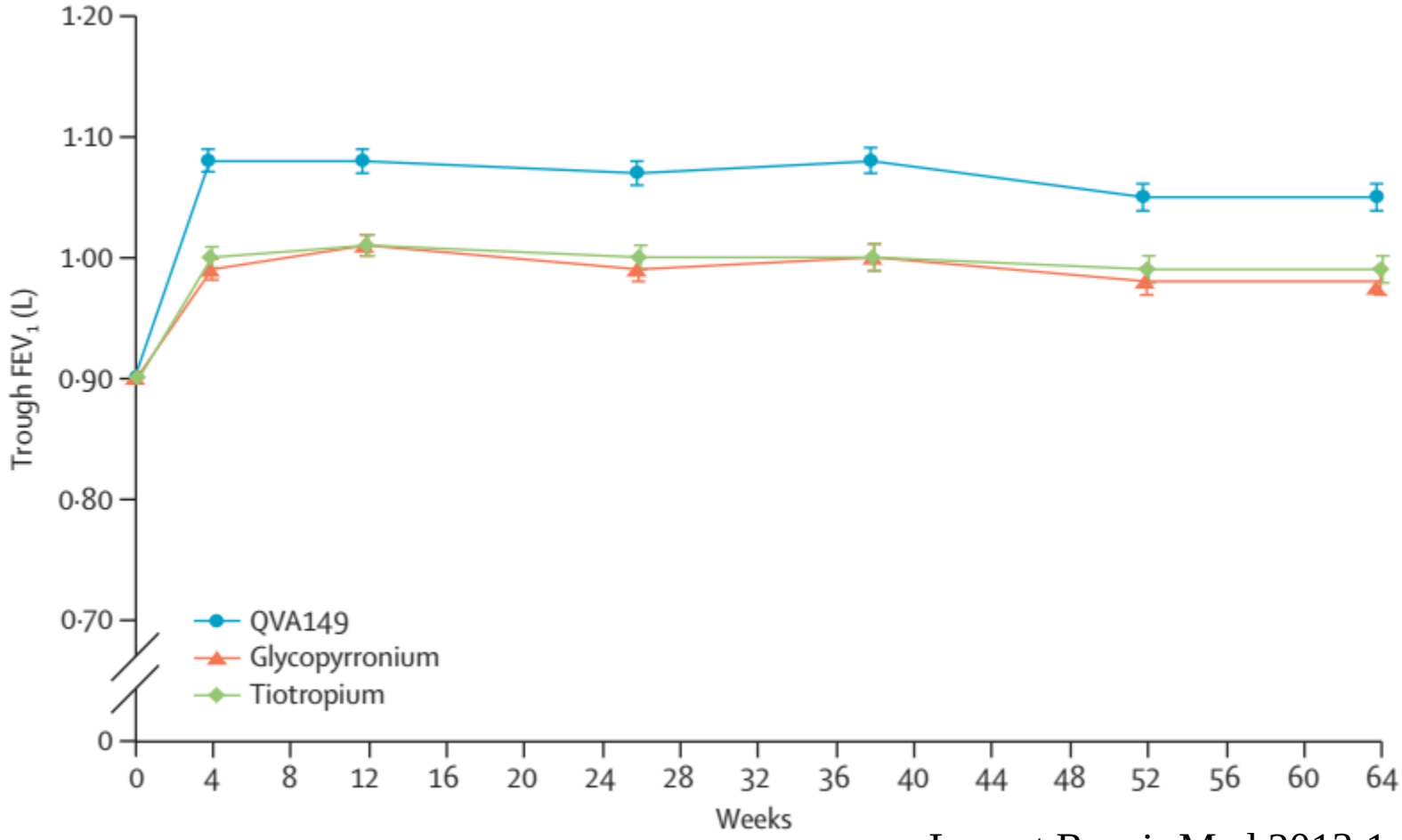


	QVA149 (n=729)	Glycopyrronium (n=740)	Tiotropium (n=737)
Age (years)	63·1 (8·1)	63·1 (8·0)	63·6 (7·8)
Men	556 (76%)	542 (73%)	553 (75%)
Race			
White	594 (81%)	605 (82%)	613 (83%)
Asian	89 (12%)	92 (12%)	79 (11%)
Black	4 (1%)	5 (1%)	7 (1%)
Other	42 (6%)	38 (5%)	38 (5%)
Severity of airflow limitation			
Severe*	578 (79%)	584 (79%)	581 (79%)
Very severe	150 (21%)	155 (21%)	156 (21%)
Duration of COPD (years)	7·2 (5·8)	7·1 (5·3)	7·2 (5·5)
Number of COPD exacerbations in previous year			
0	8 (1%)	13 (2%)	11 (1%)
1	557 (76%)	572 (77%)	552 (75%)
≥2	164 (22%)	155 (21%)	174 (24%)
Inhaled corticosteroid use at baseline	546 (75%)	557 (75%)	559 (76%)
Current smoker	277 (38%)	283 (38%)	270 (37%)
Estimated pack-years	45 (23)	44 (23)	47 (28)
Prebronchodilator FEV_1 (L)	0·91 (0·30)	0·90 (0·30)	0·89 (0·30)
Postbronchodilator FEV_1 (L)	1·04 (0·30)	1·04 (0·30)	1·04 (0·30)
Postbronchodilator FEV_1 (% predicted)	37·0% (8·1)	37·3% (8·1)	37·4% (8·1)
Pre/postbronchodilator FEV_1 reversibility (%)	17·2% (19·6)	18·8% (19·1)	18·9% (19·3)
FEV_1/FVC (%), post-bronchodilator	39·3% (9·2)	39·3% (9·6)	39·3% (9·6)
SGRQ total score at baseline†	53 (18)	52 (18)	52 (17)
Use of rescue salbutamol at baseline (puffs per day)‡	5·7 (4·6)	5·7 (5·0)	5·5 (4·7)

Group B,D

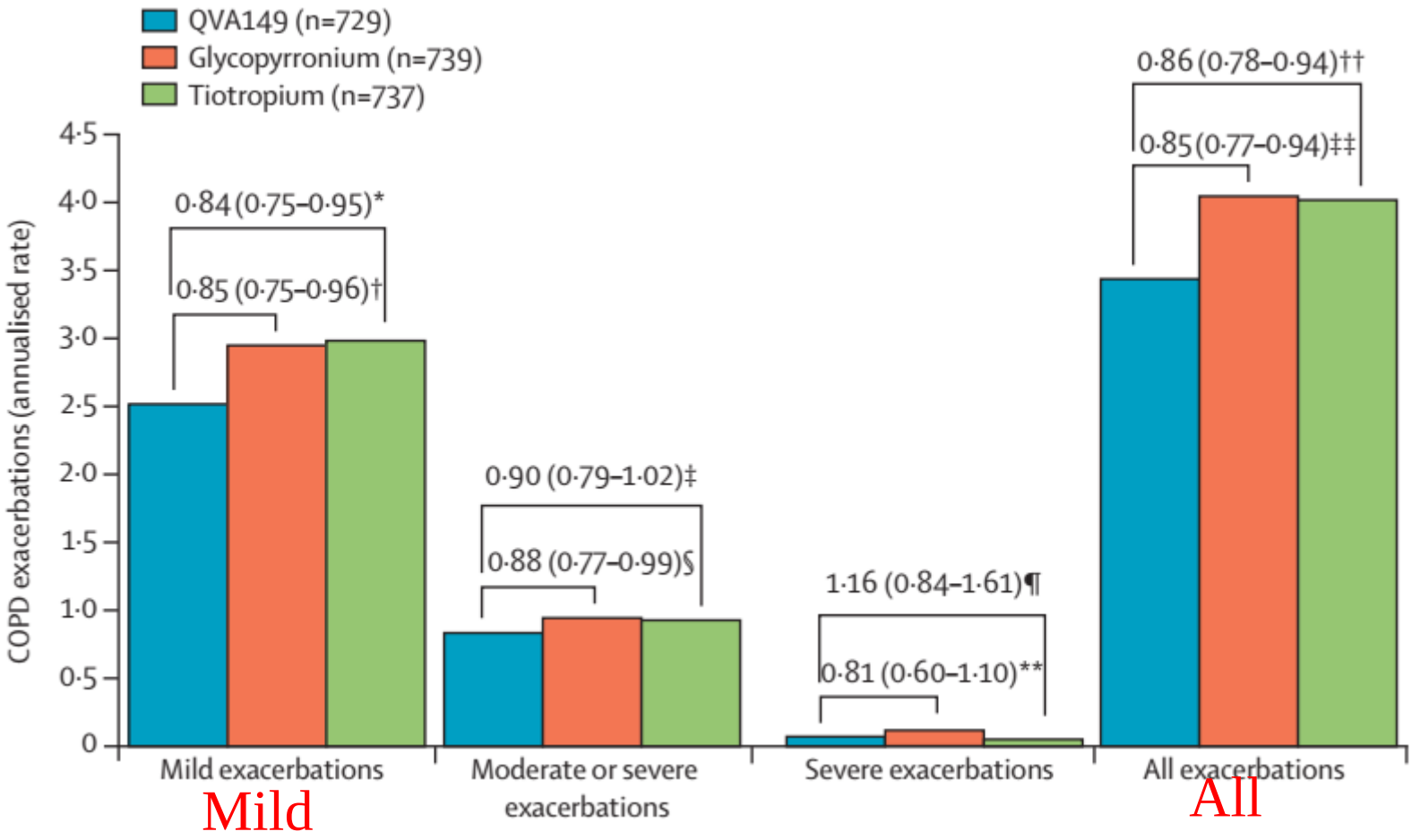
Lancet Respir Med 2013;1: 199–209

Trough FEV1 improvement



Lancet Respir Med 2013;1: 199–209

COPD exacerbation



Lancet Respir Med 2013;1: 199–209

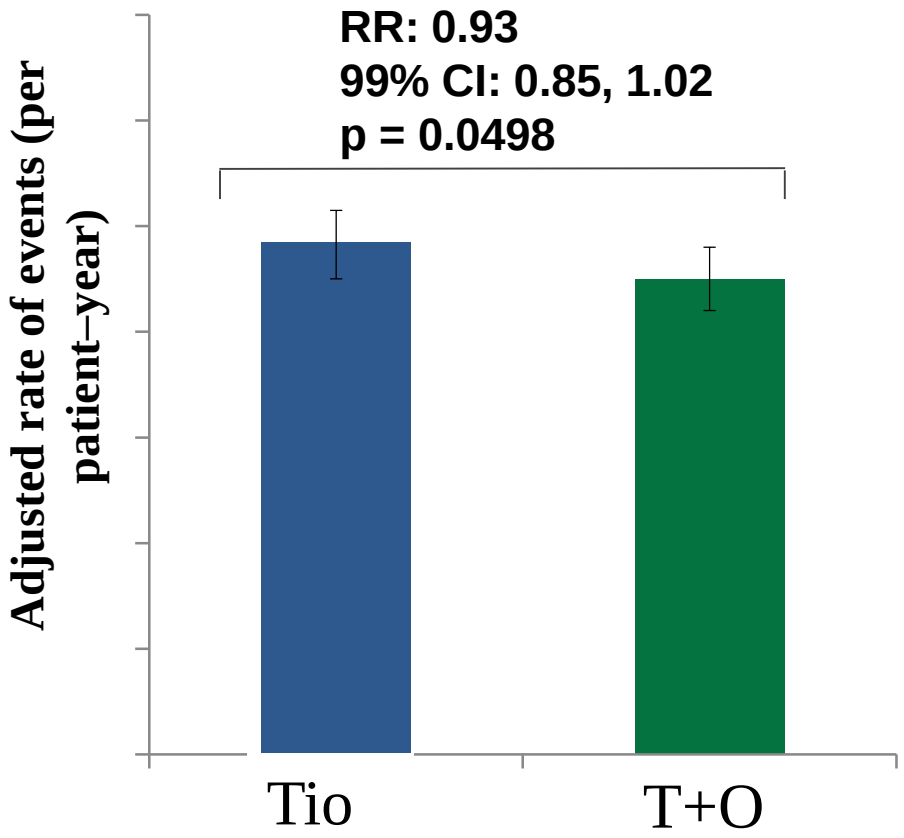
Eur Respir J 2013; 42: 1484–1494

No obvious increased adverse event with dual bronchodilator

	Placebo	QVA149 110/50 µg	Indacaterol 150 µg	Glycopyrronium 50 µg	Tiotropium 18 µg
Subjects n	232	474	476	473	480
Patients with any adverse event	134 (57.8)	261 (55.1)	291 (61.1)	290 (61.3)	275 (57.3)
COPD	91 (39.2)	137 (28.9)	153 (32.1)	150 (31.7)	138 (28.8)
Nasopharyngitis	23 (9.9)	31 (6.5)	35 (7.4)	46 (9.7)	40 (8.3)
Cough	8 (3.4)	26 (5.5)	38 (8.0)	18 (3.8)	21 (4.4)
Upper respiratory tract infection	13 (5.6)	20 (4.2)	32 (6.7)	20 (4.2)	24 (5.0)
Oropharyngeal pain	7 (3.0)	17 (3.6)	7 (1.5)	10 (2.1)	10 (2.1)
Viral upper respiratory tract infection	7 (3.0)	15 (3.2)	11 (2.3)	13 (2.7)	12 (2.5)
Bacterial upper respiratory tract infection	13 (5.6)	10 (2.1)	13 (2.7)	15 (3.2)	22 (4.6)
Lower respiratory tract infection	5 (2.2)	9 (1.9)	15 (3.2)	7 (1.5)	12 (2.5)
Back pain	5 (2.2)	8 (1.7)	11 (2.3)	17 (3.6)	8 (1.7)
Serious adverse events	13 (5.6)	22 (4.6)	26 (5.5)	29 (6.1)	19 (4.0)
Adjudicated CCV events					
Atrial fibrillation/flutter, new onset	0	2 (0.4)	3 (0.6)	2 (0.4)	1 (0.2)
Serious CCV events	1 (0.4)	0	6 (1.3)	7 (1.5)	4 (0.8)
MACE	0	0	2 (0.4)	3 (0.6)	3 (0.6)
Nonfatal myocardial infarction	0	0	0	1 (0.2)	0
Nonfatal stroke	0	0	1 (0.2)	0	2 (0.4)
Heart failure requiring hospitalisation	0	0	1 (0.2)	1 (0.2)	0
Coronary revascularisation[#]	0	0	0	1 (0.2)	2 (0.4)
Non-MACE	1 (0.4)	0	4 (0.8)	6 (1.3)	3 (0.6)
Deaths[¶]	0	1 (0.2)	2 (0.4)	1 (0.2)	3 (0.6)
Discontinuations					
Due to an adverse event	10 (4.3)	6 (1.3)	24 (5.0)	14 (3.0)	10 (2.1)
Due to a SAE	3 (1.3)	3 (0.6)	11 (2.3)	6 (1.3)	5 (1.0)

Decreased moderate-to- severe COPD exacerbation during the actual treatment period

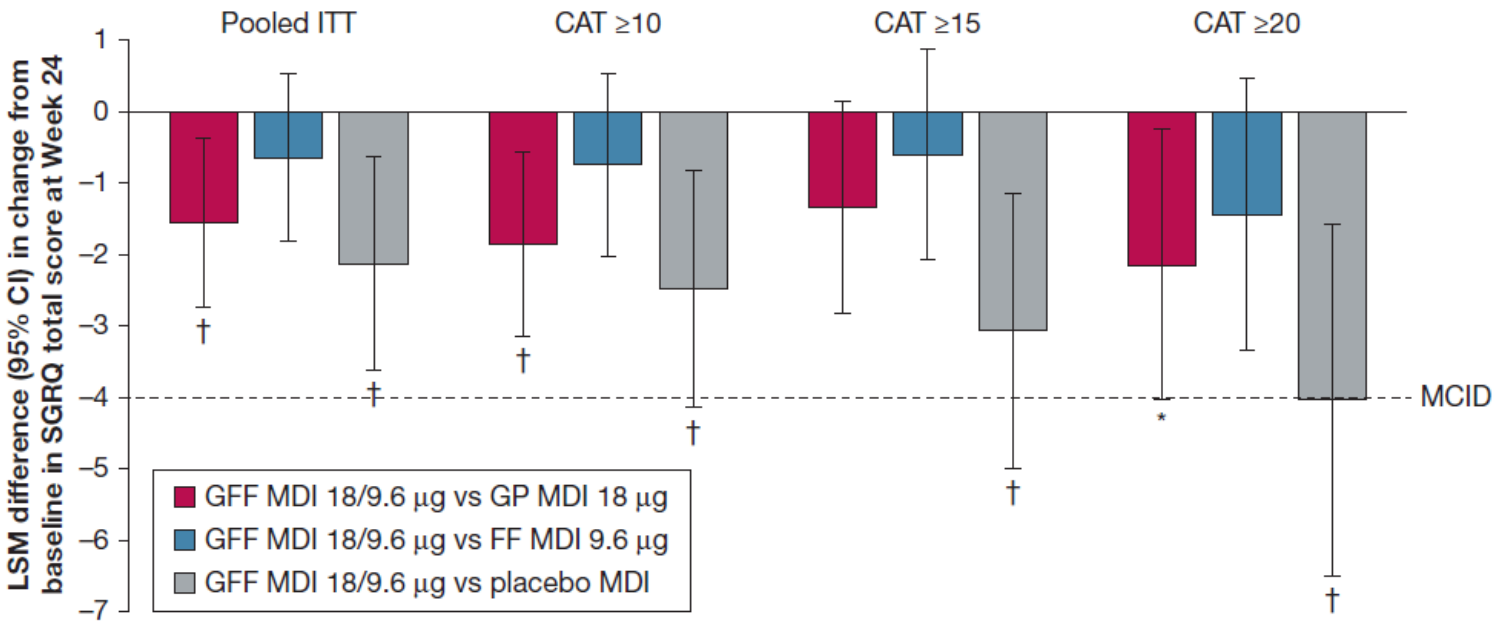
	Tio 5 µg	T+O 5/5 µg
Number of treated patients, n	3941	3939
Total number of moderate-to-severe COPD exacerbations, n	2975	2937
Adjusted[1] rate of events, per patient–year		
Mean (SE)	0.97 (0.026)	0.90 (0.026)
99% CI	0.90, 1.03	0.84, 0.96
RR of events vs Tio 5 µg		
Mean (SE)	0.93 (0.036)	
99% CI	0.85, 1.02	
p-value	0.0498	



Calverley PMA et al. Lancet Respir Med. 2018 Mar 28. pii: S2213-2600(18)30102-4

LAMA/LABA is considered when patients are highly symptomatic

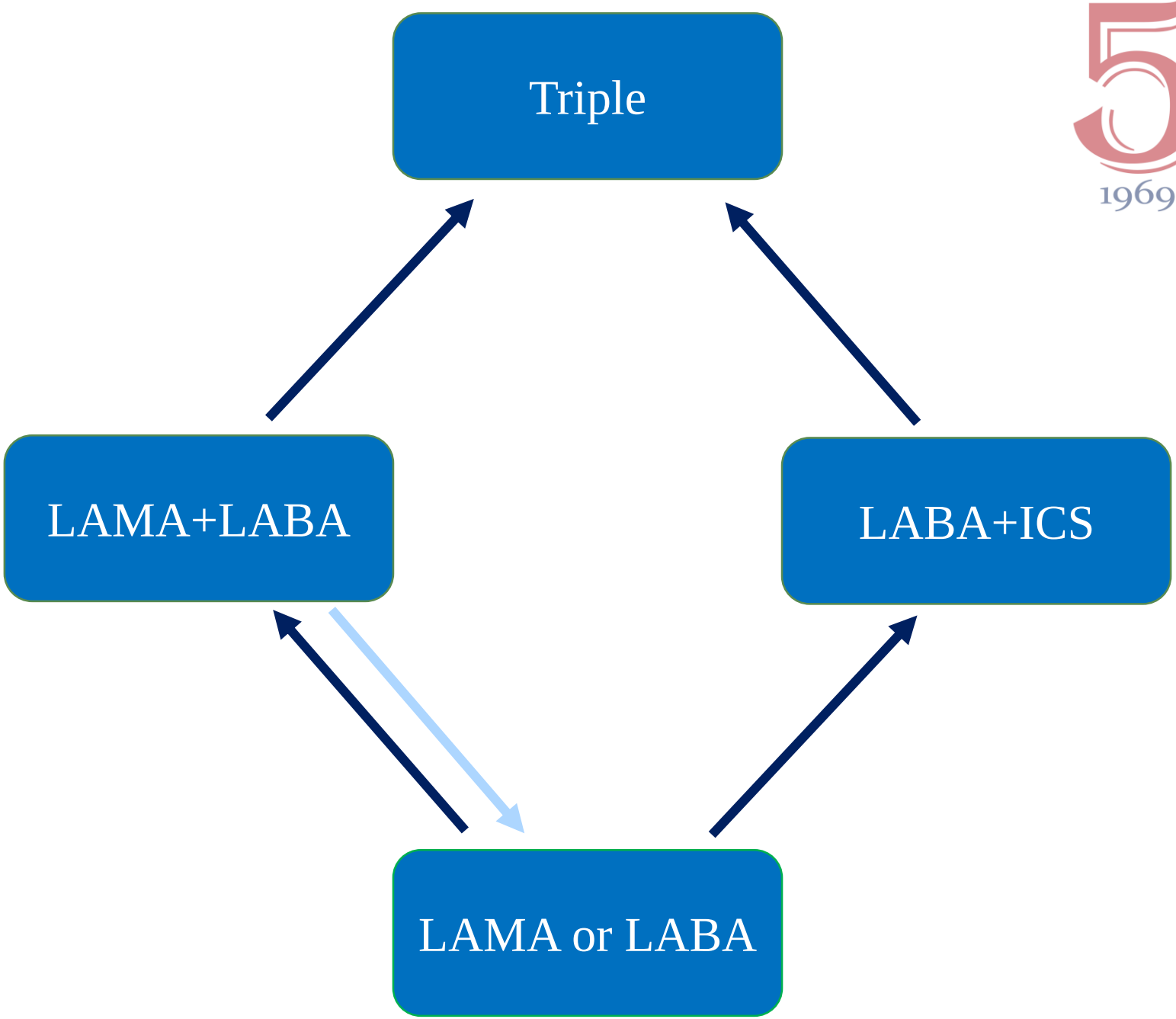
(GLY/FOR vs. mono components)



CHEST 2017; 152(6):1169-1178

Conclusion

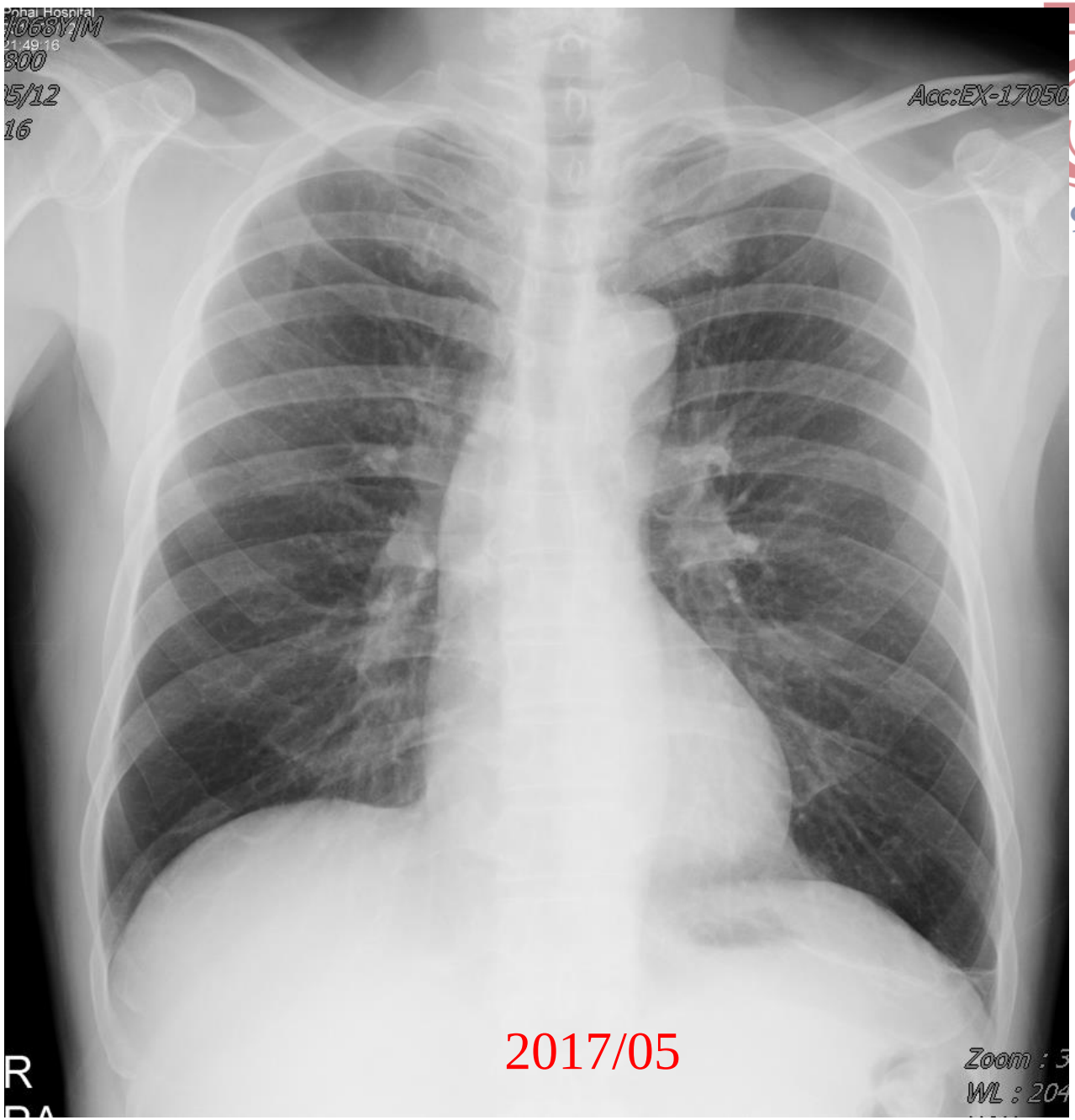
- The guideline suggests dual bronchodilators in more symptomatic patients or those who responds to mono-bronchodilator poorly
- If a patient receives dual bronchodilator, no step down needed due to
  - Better improvement of pulmonary functions, respiratory symptoms, quality of life and AE?
  - No increase adverse events
  - Price


Triple
LAMA+LABA
LABA+ICS
LAMA or LABA

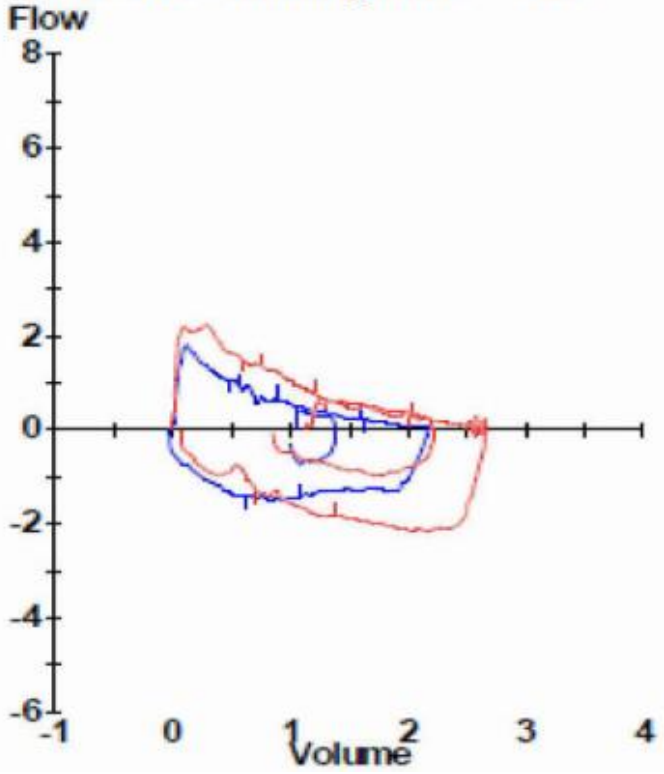
- 1. ICS tapering
- 2. Dual therapy → monotherapy
- 3. Triple therapy → combination therapy

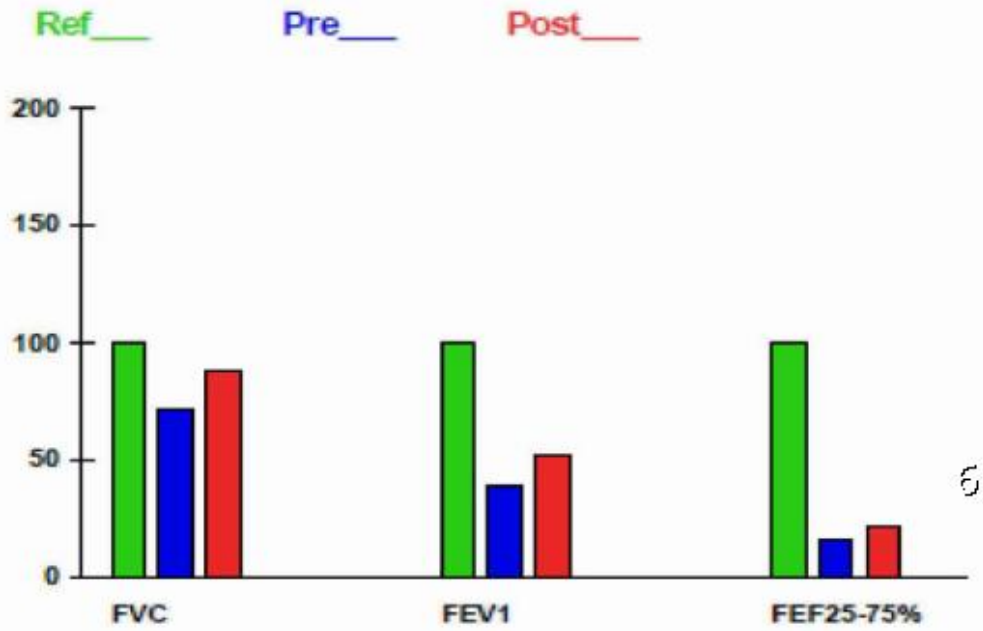
- 胡先生 69M
- Chronic cough with few sputum for weeks
- Smoking: 1PPD since 20y/o
- Occupation: retired public servant
- Systemic disease: denied

- Con’s: clear
- Vital signs: no fever
- Chest: wheezing
- Ext: no obvious clubbing finger


Acc:EX-17050
2017/05

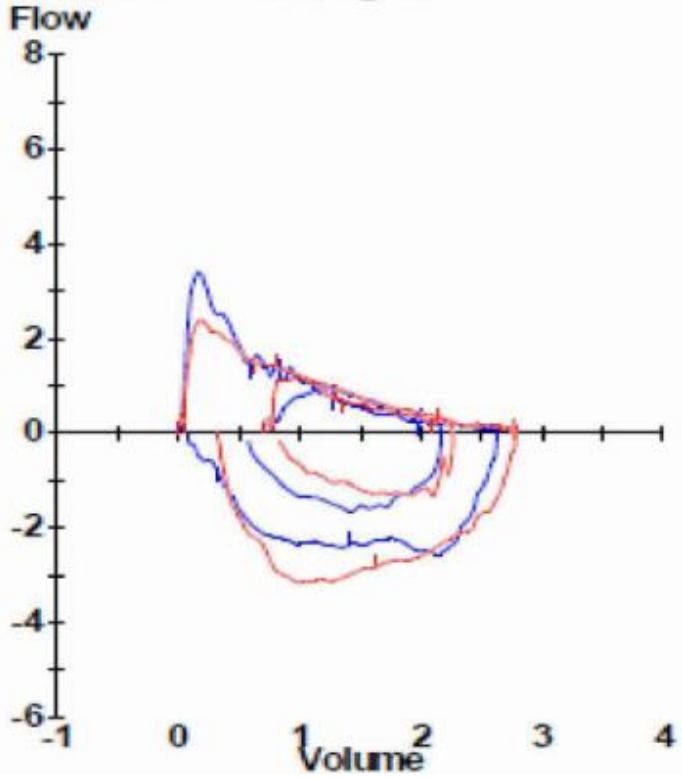
Spirometry		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	3.03	2.17	71	2.66	88	23
FEV1	Liters	2.41	0.93	39	1.25	52	34
FEV1/FVC	%	80	43		47		
FEF25-75%	L/sec	2.51	0.40	16	0.54	21	34
PEF	L/sec	7.05	1.79	25	2.24	32	25
FVL ECode			111010		111000		
Lung Volumes							
TLC	Liters	5.25	5.63	107	6.15	117	9
VC	Liters	3.03	2.19	72	2.66	88	22
RV	Liters	2.14	3.44	161	3.49	163	1
RV/TLC	%	40	61		57		
FRC PL	Liters	3.19	3.91	123	4.15	130	6
Diffusion							
DLCO	mL/mmHg/min	16.6	10.9	65			
DLCO/VA	mL/mHg/min/L	3.66	3.20	87			

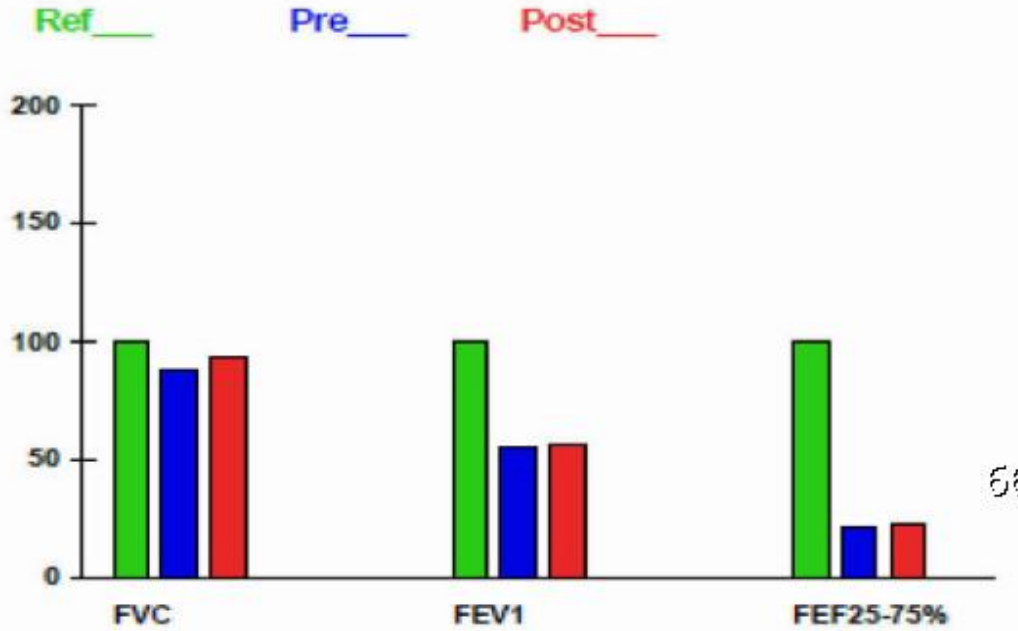




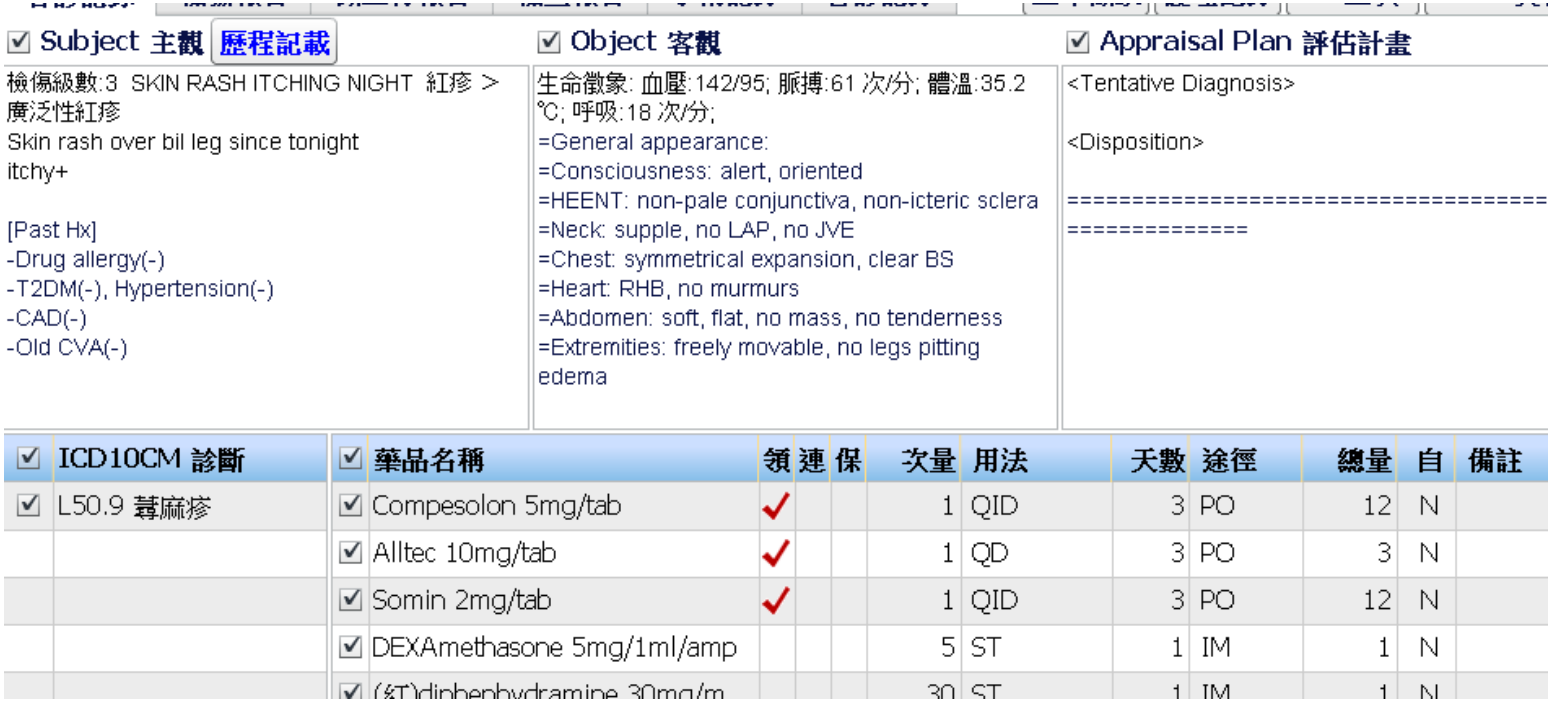
2017/5

Spirometry		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	3.00	2.63	88	2.79	93	6
FEV1	Liters	2.38	1.30	55	1.33	56	2
FEV1/FVC	%	80	49		47		
FEF25-75%	L/sec	2.47	0.52	21	0.57	23	10
PEF	L/sec	7.01	3.40	48	2.39	34	-29
FVL ECode			111010		000010		
Lung Volumes							
TLC	Liters	5.23	5.94	113	6.17	118	4
VC	Liters	3.00	2.63	88	2.79	93	6
RV	Liters	2.15	3.31	153	3.38	157	2
RV/TLC	%	40	56		55		
FRC PL	Liters	3.12	4.01	129	4.10	131	2
Diffusion							
DLCO	mL/mmHg/min	17.0	11.2	66			
DLCO/VA	mL/mHg/min/L	3.67	3.53	96			





Urticaria attack



☑ Subject 主觀 歷程記載

檢傷級數:3 SKIN RASH ITCHING NIGHT 紅疹 >
廣泛性紅疹
Skin rash over bil leg since tonight
itchy+

[Past Hx]
-Drug allergy(-)
-T2DM(-), Hypertension(-)
-CAD(-)
-Old CVA(-)

☑ Object 客觀

生命徵象: 血壓:142/95; 脈搏:61 次/分; 體溫:35.2 ℃; 呼吸:18 次/分;
=General appearance:
=Consciousness: alert, oriented
=HEENT: non-pale conjunctiva, non-icteric sclera
=Neck: supple, no LAP, no JVE
=Chest: symmetrical expansion, clear BS
=Heart: RHB, no murmurs
=Abdomen: soft, flat, no mass, no tenderness
=Extremities: freely movable, no legs pitting edema

☑ Appraisal Plan 評估計畫

<Tentative Diagnosis>

<Disposition>

==========

☑	ICD10CM 診斷	☑	藥品名稱	領	連	保	次量	用法	天數	途徑	總量	自	備註
☑	L50.9 蕁麻疹	☑	Compesolon 5mg/tab	✓			1	QID	3	PO	12	N	
		☑	Alltec 10mg/tab	✓			1	QD	3	PO	3	N	
		☑	Somin 2mg/tab	✓			1	QID	3	PO	12	N	
		☑	DEXAmethasone 5mg/1ml/amp				5	ST	1	IM	1	N	
		☑	(紅)diphenhydramine 30mg/m				30	ST	1	IM	1	N	

Hb	13.4g/dL

Asthma COPD Overlap patient

IgE	578 IU/ml

Triple therapy but irregular f/u

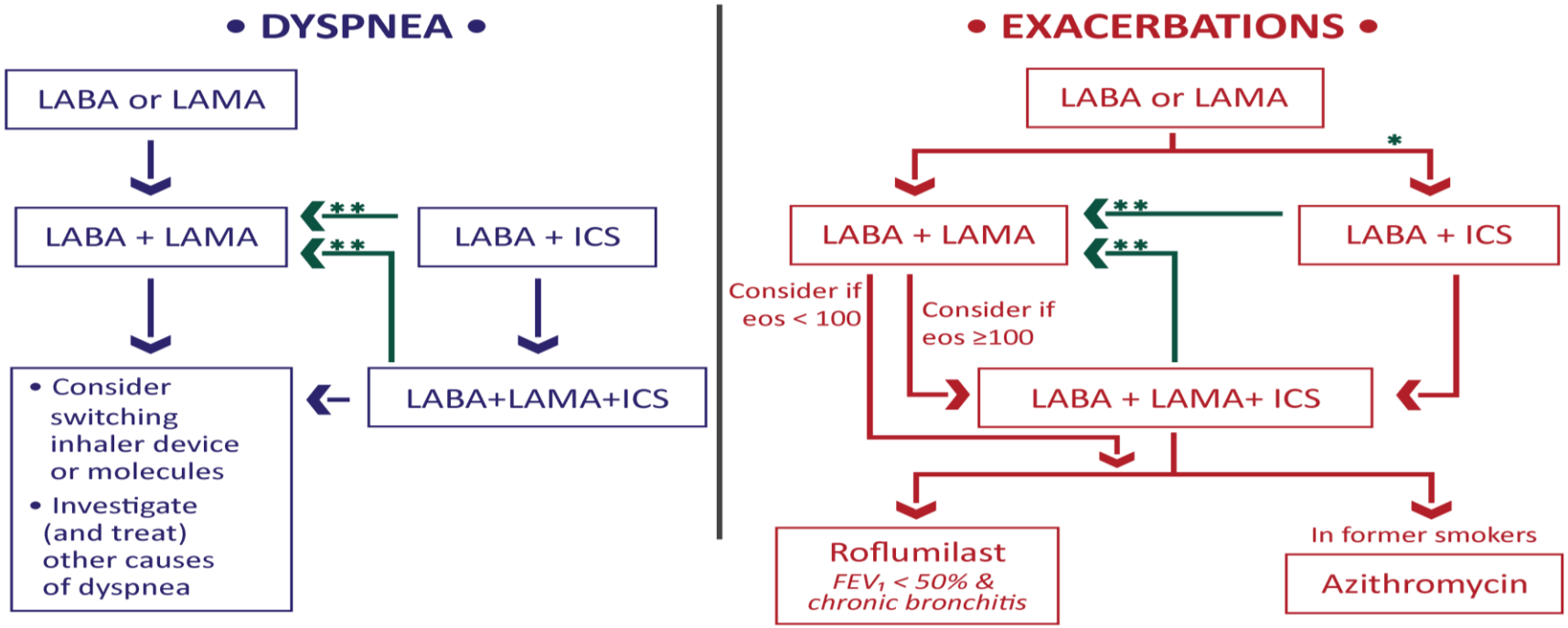
		-	-
Level date		19-05-14	19-05-14
Level time		14:54	15:03

		Pred	Pre	%(Pre/Pred)	Post	%(Po/Pred)	%CHG
FVC	L	3.06	3.10	101	3.69	121	19
FEV 1	L	2.41	1.74	72	2.23	92	28
FEV1/FVC	%	79.34	56.17	71	60.33	76	7
FEV6	L		2.96		3.45		16
MMEF	L/s	2.49	0.82	33	1.00	40	21
75/85	L/s	0.44	0.22	50	0.22	50	0
PEF	L/s	7.07	3.19	45	5.54	78	74
FET	sec		8.63		9.24		7
FVC IN	L	3.06	3.43	112	3.93	129	15
FIV1	L		2.69		3.82		42
TLC	L	6.10	7.45	122	7.42	122	-0
VC	L	3.06	3.43	112	3.93	129	15
RV	L	2.47	4.01	162	3.49	141	-13
RV%TLC	%	41.26	53.88	131	46.99	114	-13
FRCpl	L	3.40	4.65	137	4.03	119	-13
ERV	L	0.93	0.64	69	0.55	59	-15
DLCO_SB ml/(min*mmHg)		24.04	16.84	70			
DLCO/VAml/(min*mmHg*L)		4.22	2.59	61			
VA_SB	L	5.85	6.51	111			

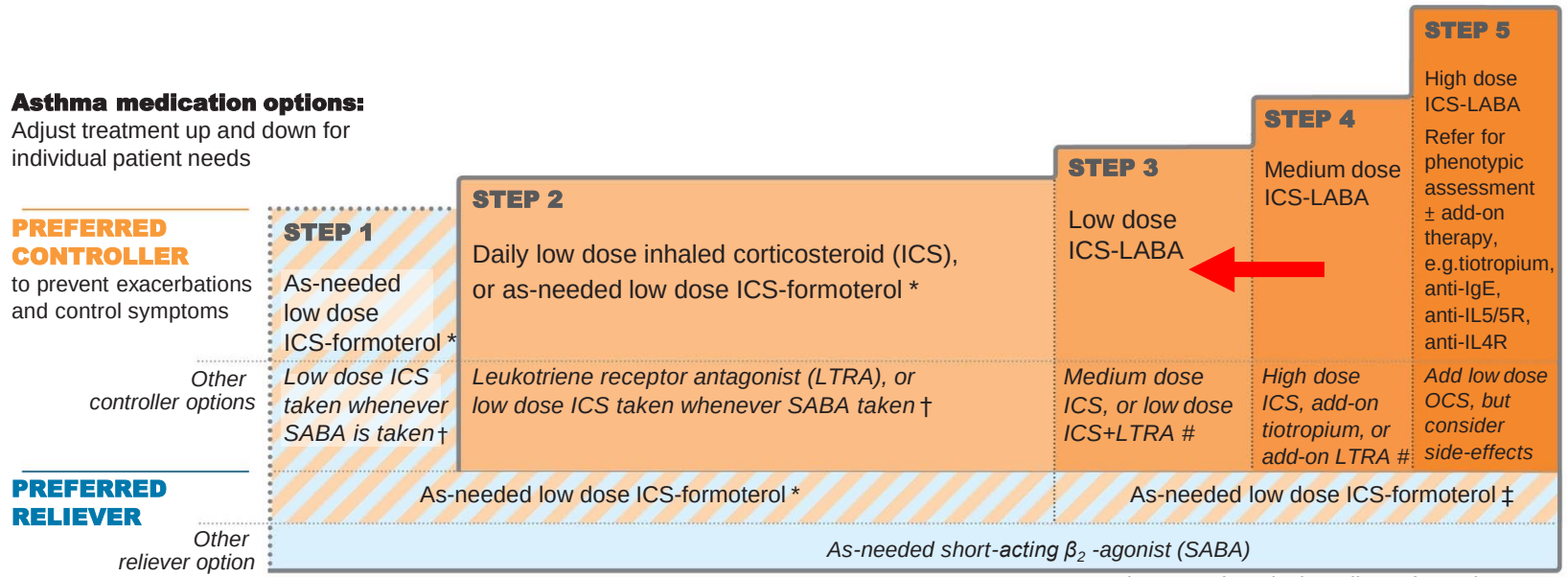
2019/5

Follow-up Treatment

1. **IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.**
2. **IF NOT:**
   - ✓ Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - ✓ Place patient in box corresponding to current treatment & follow indications
   - ✓ Assess response, adjust and review
   - ✓ These recommendations do not depend on the ABCD assessment at diagnosis



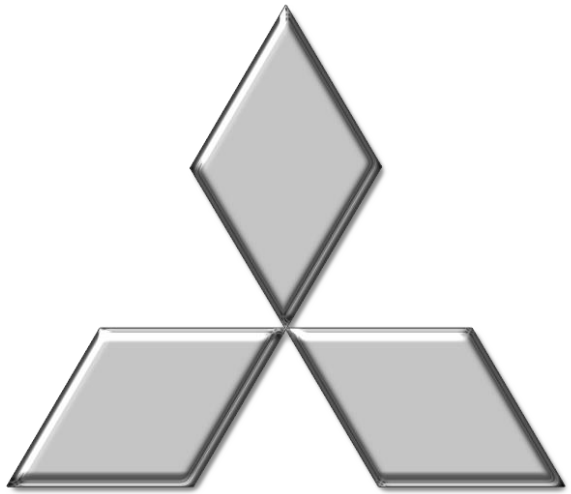
eos = blood eosinophil count (cells/µL)
** Consider if eos ≥ 300 or eos ≥ 100 AND ≥2 moderate exacerbations / 1 hospitalization*
*** Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS*

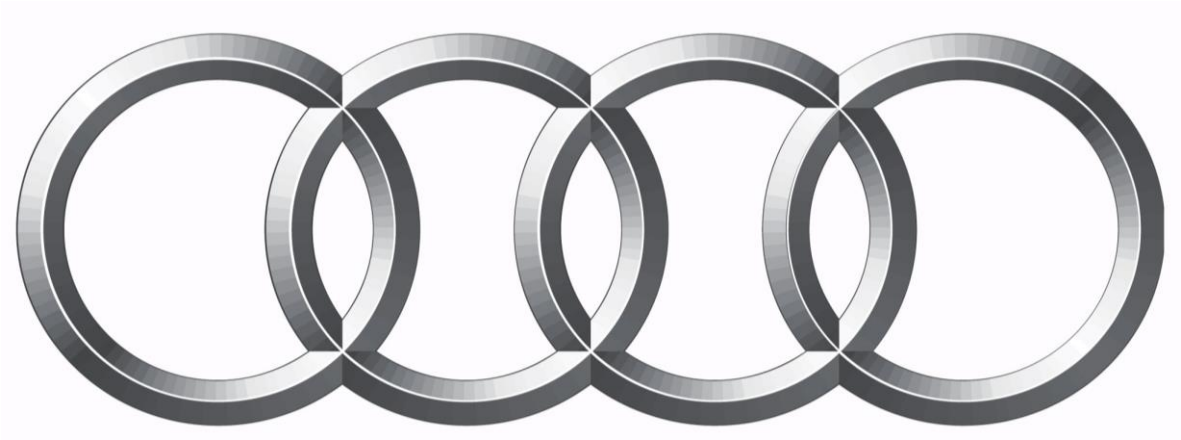


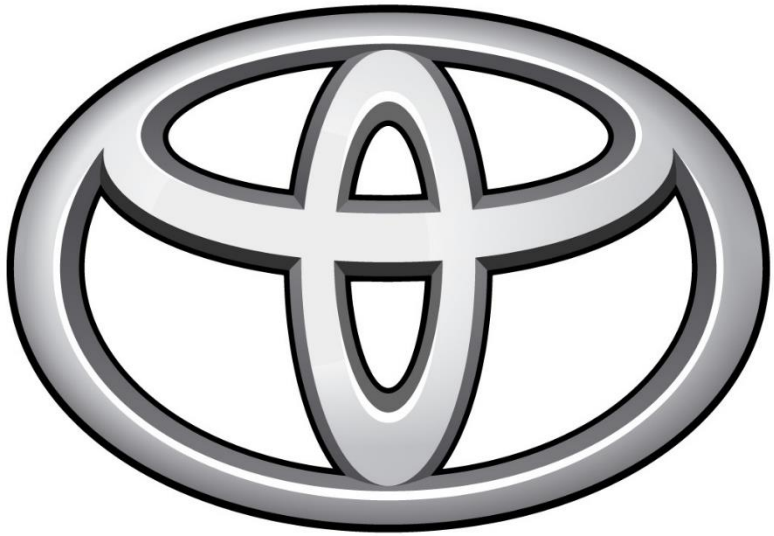
* Off-label; data only with budesonide-formoterol (bud-form)
† Off-label; separate or combination ICS and SABA inhalers
‡ Low-dose ICS-form is the reliever for patients prescribed bud-form or BDP-form maintenance and reliever therapy
\# Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV >70% predicted

Conclusion

- Triple therapy may de-escalate to combination in ACOS by GINA guideline, yet more evidence is needed





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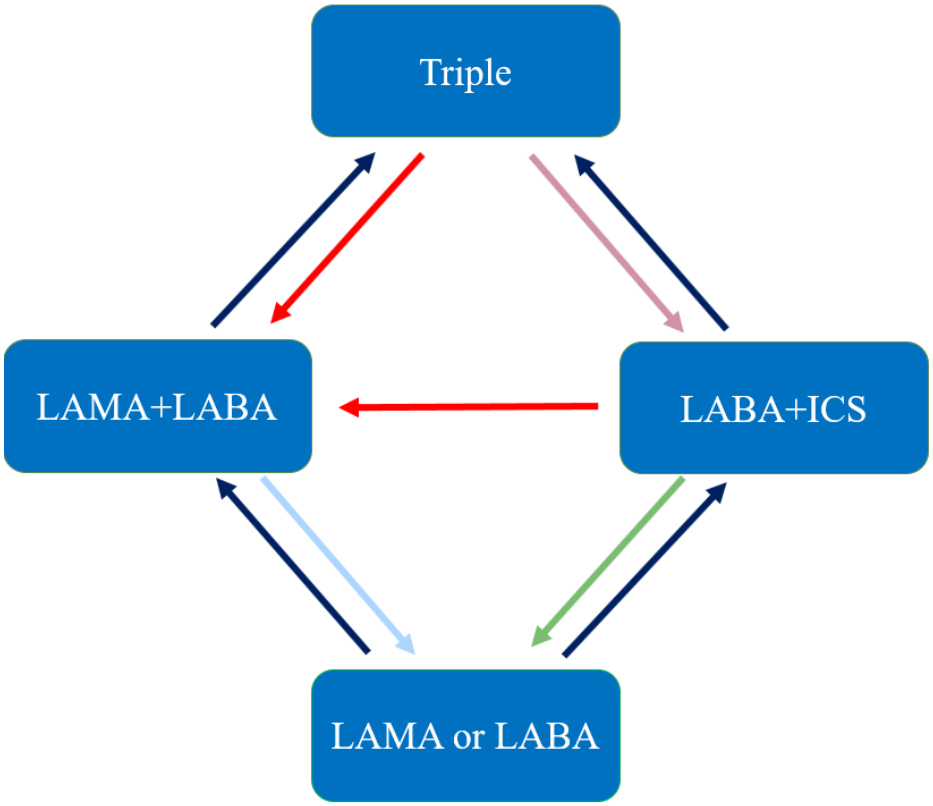
Conclusion

- Eosinophil count plays an important role in COPD exacerbation and ICS response
- There are evidences for de-escalation treatments in low risk patients



Thank You