

# אֲהַזֵּע קְפָוָעָה רְגִוָּה?

האיגוד הישראלי לרפואה פנימית  
ISRAEL SOCIETY OF INTERNAL MEDICINE



## What's New

31.3-2.4.2022 | מלון דן כרמל, חיפה

# כֶּאֶכֶ' צָמֵה כְּלִיְקָרְקָר

מנהל מחלקה פנימית ד'  
רופא בכיר - מכון הריאה  
מרכז רפואי הדסה עין כרם

# **כינור רקות**

יעוז – BI, AZI, GSK, סנופי.

הרצאות מטעם – GSK, נוברטיס, AZI, רפואי,  
מגה-פארם, טבע, BI, קמהදע.

כנסים בסיווע – נוברטס, AZI, GSK, רפואי, רוש.

**ההרצאה היום אינה ללא חסות ישירה**

# מה זה רזאכ...?

- חיזואים גסומתא - דקה וקלה
- חיזואים נאוחת כיאת כירוכסז'ינט (ILD)
- חיזואים ג-COPD
- חיזואים גסקידת נוקראנת סרור כיאת

אֵה מְסֻתָּה  
אֲזַהֲרָה ?





GLOBAL STRATEGY FOR  
ASTHMA MANAGEMENT AND PREVENTION

Updated 2020

© 2020 Global Initiative for Asthma

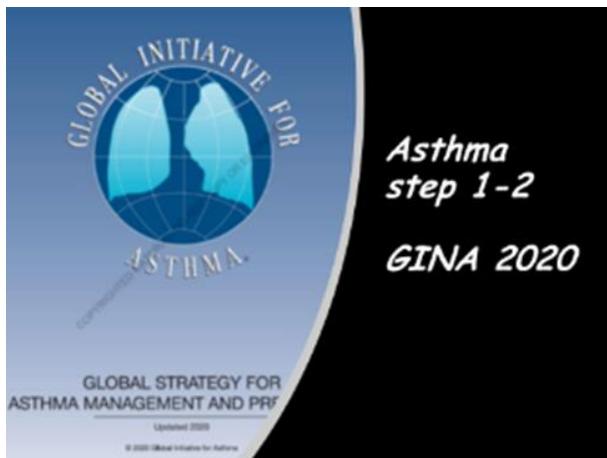
**Asthma  
step 1 - 2**

**GINA 2020**

# הכלי הראשון לטיפול באסתמה

## כטטאה כ Step 1-2

- עבודות קודמות על שיטת SMART  
Single Maintenance & Reliever Therapy
- כל חולן האסתמה, אפילו הקלים שבהם, בסיכון להתקhcיות  
קשהות של מחלתם
- ברונcodילטציה באמצעות FORMOTEROL (סוג של LABA)  
מהירה כמו עזרת Ventolin.
- בעקבות כך – עבודות הראו שילוב של  
ICS-Formoterol (ונטולין) לפי הצורך עדיף על  
SABA (ונטולין) לפי הצורך.

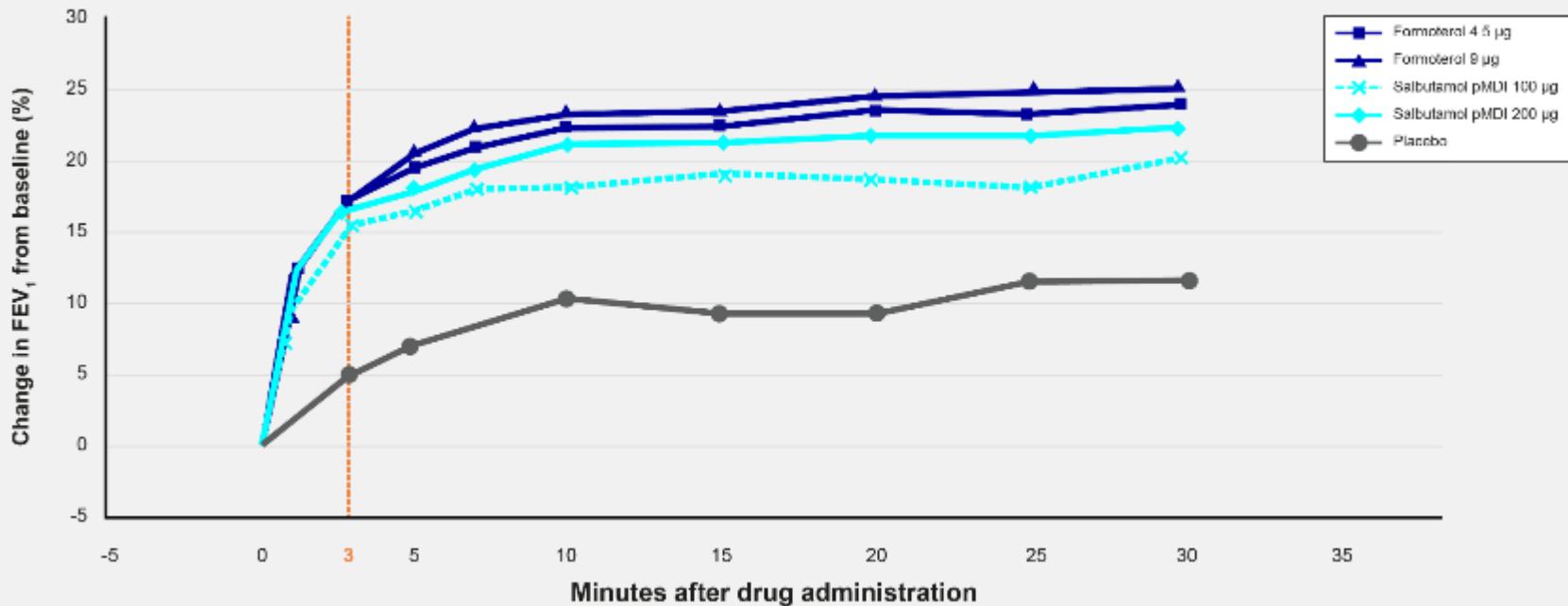


# Patients with mild asthma are at risk of exacerbations

**19–36% of patients with mild asthma experience an exacerbation every year**

	Study	Study type	Definition of exacerbation	Total number of patients	% experiencing an exacerbation within previous 12m
2001	O'Byrne et al. <sup>1</sup> (OPTIMA)*	Randomised clinical trial	Severe exac: OCS use, hospitalisation/ emergency treatment, >25% decrease from baseline in morning PEF on 2 consecutive days	Group A (placebo) –237	33.3
				Group B (budesonide 200 µg) –317	33.8
2014	Price et al. <sup>2</sup> (REALISE)	Quantitative questionnaire	Acute exac: ≥1 course of OCS in the previous 12 months	Reliever only – 1419	26.1
				Single-drug preventer inhaler –1923	29.2
2017	Ding et al. <sup>3</sup>	Observational survey	Physician confirmed worsening of symptoms	1115	19
2018	Bloom et al. <sup>4†</sup>	Population-based cohort study	≤300 mg OCS, A&E visit or hospitalisation	BTS Step 1 – 86360	31
				BTS Step 2 – 54773	36
2018	O'Byrne et al. <sup>5</sup> (SYGMA 1)	Randomised clinical trial	Severe exac: ≥3 days OCS use, hospitalisation or ED visit	3836	19.7
2018	Bateman et al. <sup>6</sup> (SYGMA 2)	Randomised clinical trial	Severe exac: ≥3 days OCS use, hospitalisation or ED visit	4176	22

# Onset of bronchodilation with formoterol vs salbutamol



Randomised, double-blind, double-dummy, placebo-controlled and cross-over study (n=36).

FEV<sub>1</sub>, forced expiratory volume in 1 second; pMDI, pressurised metered dose inhaler.

Adapted from Seberová E, et al. Respir Med 2000;94:607–11.

Improvement in FEV<sub>1</sub> from baseline is as rapid and effective with formoterol 4.5 or 9 µg as with salbutamol 100 or 200 µg

## Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma

Paul M. O'Byrne, M.B., J. Mark FitzGerald, M.D., Eric D. Bateman, M.D., Peter J. Barnes, M.D., Nanshan Zhong, Ph.D., Christina Keen, M.D., Carin Jorup, M.D., Rosa Lamarka, Ph.D., Stefan Ivanov, M.D., Ph.D., and Helen K. Reddel, M.B., B.S., Ph.D.

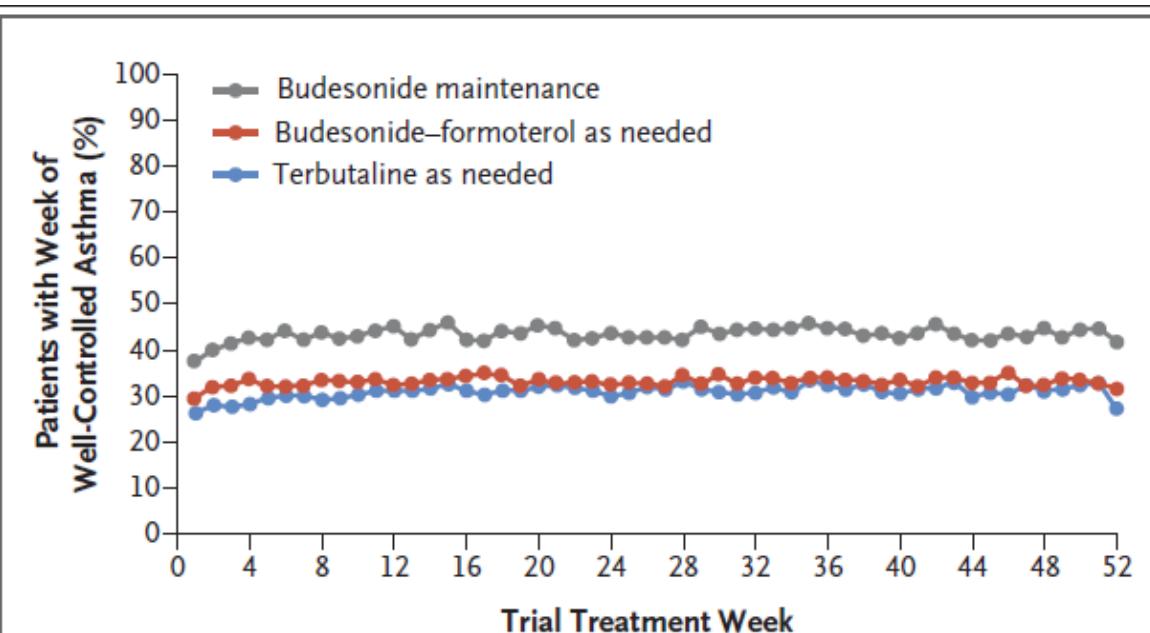
### **Primary endpoint:**

**Budesonide–formoterol used as needed was superior to terbutaline (34.4% vs. 31.1% of weeks well controlled; odds ratio, 1.14; 95% confidence interval [CI], 1.00 to 1.30; P = 0.046).**

**Table 2.** Summary of Asthma Exacerbations, According to Treatment Group.

Variable	Terbutaline as Needed (N=1277)	Budesonide–Formoterol as Needed (N=1277)	Budesonide Maintenance Therapy (N=1282)
All severe exacerbations			
Patients with $\geq 1$ exacerbation — no. (%)	152 (11.9)	71 (5.6)	78 (6.1)
Total no. of exacerbations	188	77	89
Annualized exacerbation rate	0.20	0.07	0.09
Comparison between as-needed budesonide–formoterol and other regimen			
Rate ratio	0.36	—	0.83
95% CI	0.27–0.49	—	0.59–1.16
P value	<0.001	—	0.28

## המחיר – ירידת מסויימת בשליטה על הסמפטומים



**Figure 2.** Overall Weeks of Well-Controlled Asthma, According to Data in the Electronic Diary.



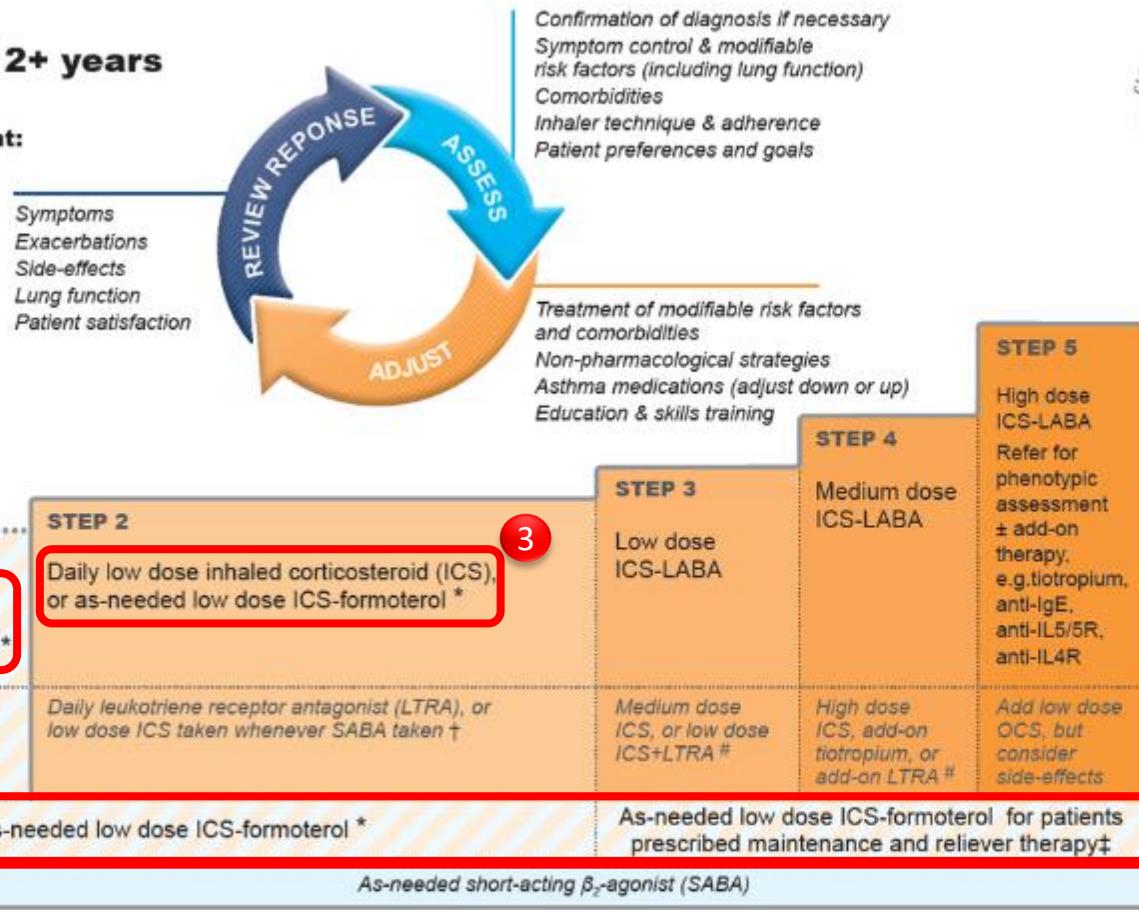
Box 3-5A

## Adults & adolescents 12+ years

### Personalized asthma management:

Assess, Adjust, Review response

## GINA 2020



\* Data only with budesonide-formoterol (bud-form)

† Separate or combination ICS and SABA inhalers

‡ Low-dose ICS-form is the reliever only for patients prescribed bud-form or BDP-form maintenance and reliever therapy

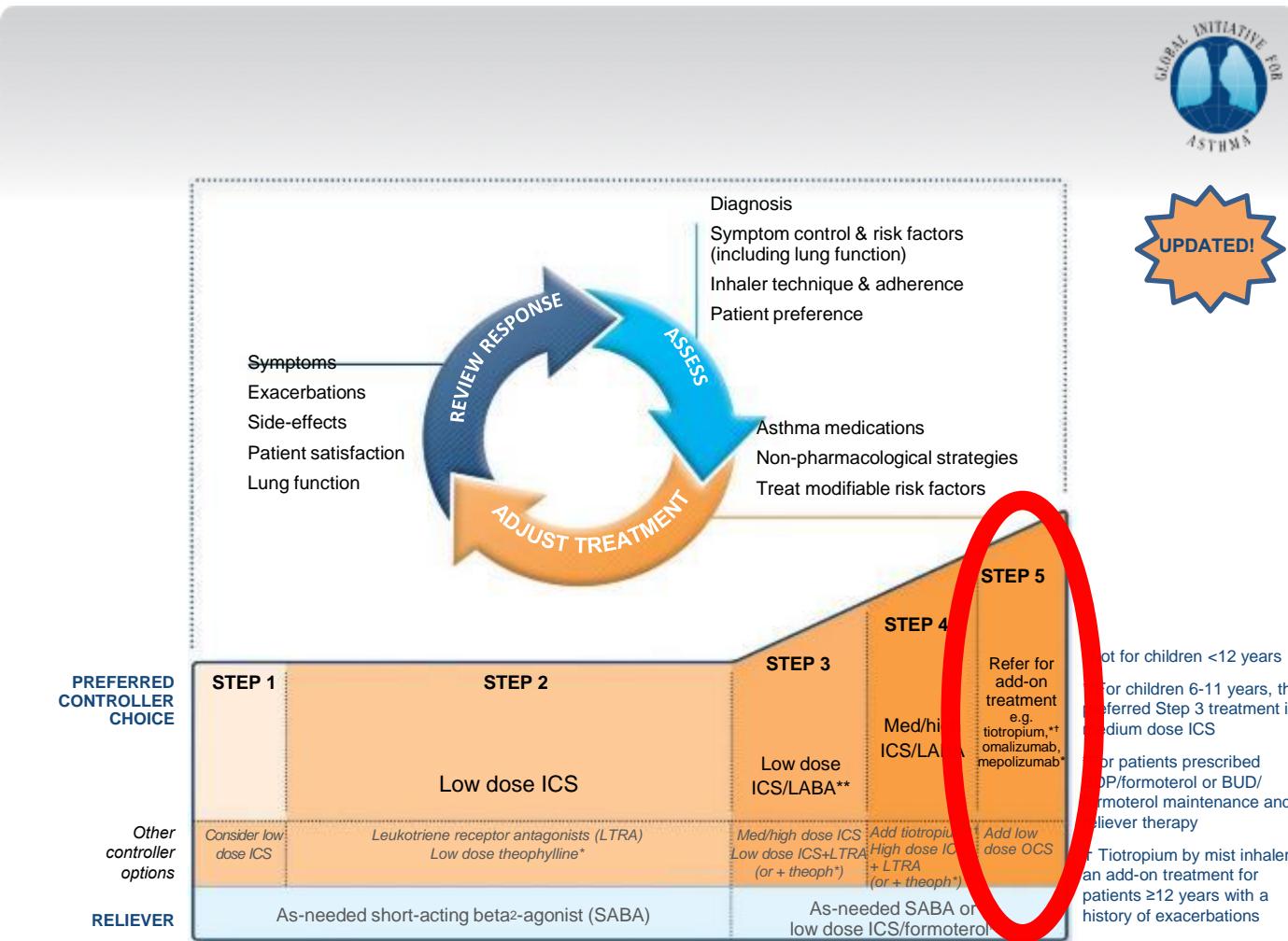
# Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 >70% predicted

# OUTDATED STUFF!





**UPDATED!**



# ERS/ATS guideline definition of severe asthma



"Asthma which requires treatment with high-dose ICS plus a second controller medication (and/or systemic corticosteroids) to prevent it from becoming 'uncontrolled' or which remains 'uncontrolled' despite this therapy"

Uncontrolled asthma can be defined by one or more of the following:



Poor symptom control



Frequent severe exacerbations



Serious exacerbations

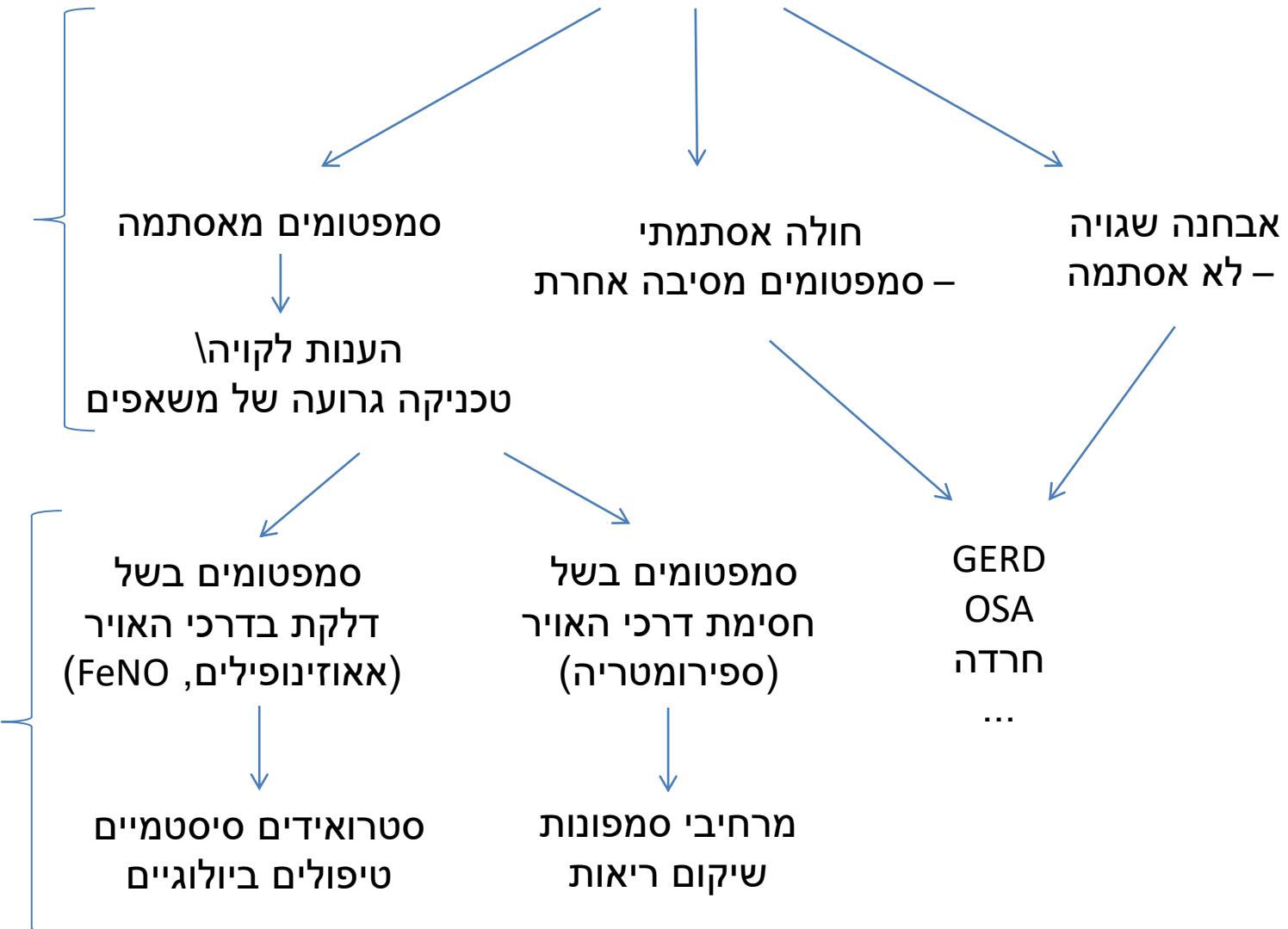


Airflow limitation

# אסתמה קשה – סטטוס איסטמי

## פאלומות ויכוח גאנזאים

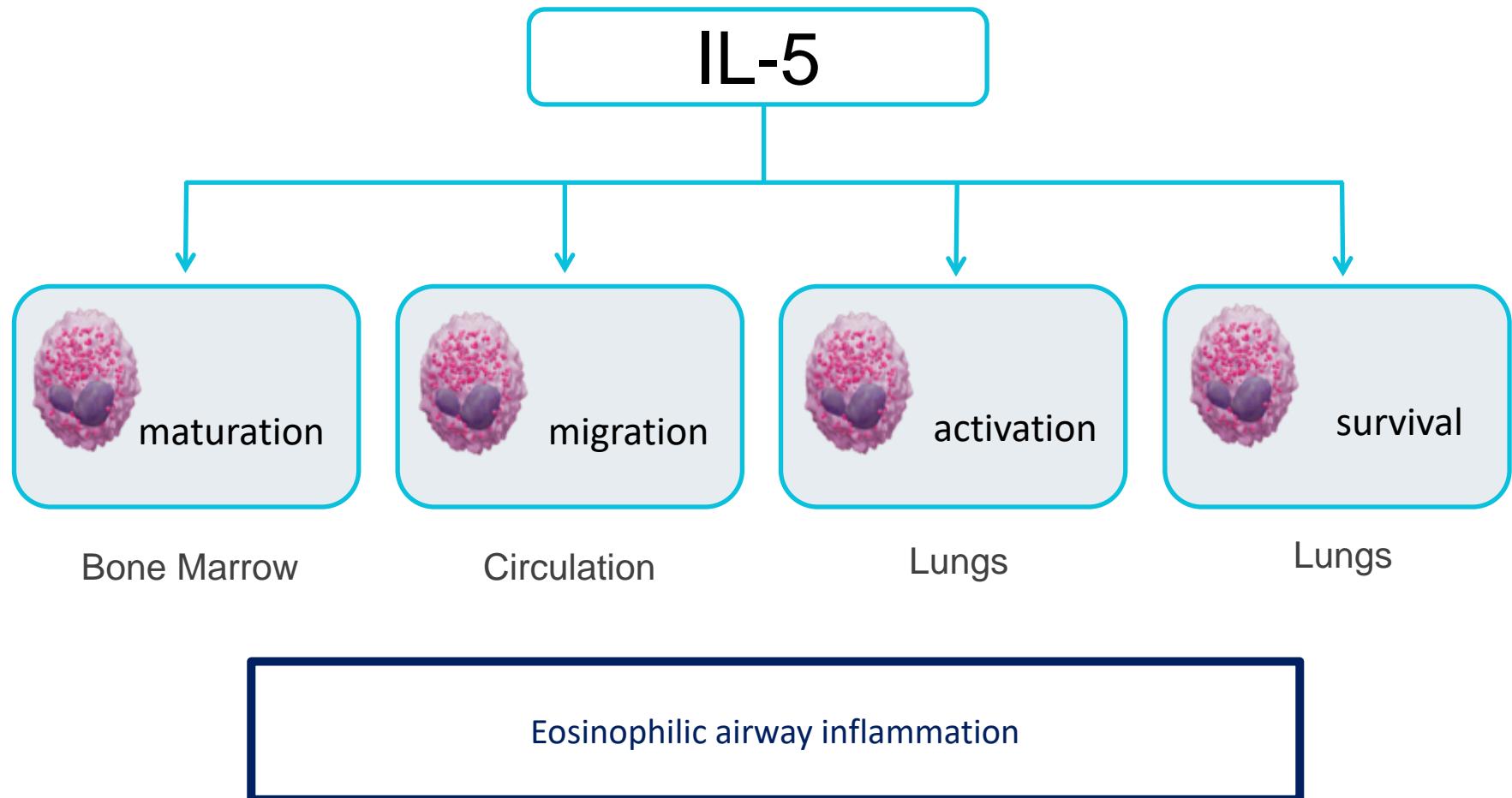
### **Difficult Asthma**



# Severe asthma - treatment options

- Methotrexate, cyclosporine, azathiaprine
- Spiriva (tiotropium)
- Omalizumab (Xolair)
- anti-TNF (Enbrel)
- Anti IL-5:mepolizumab, Benralizumab, Reslizumab
- Anti IL-4/IL-13: dupilumab
- Anti IL-13: lebrikizumab, tralokinumab
- Anti TSLP
- Prostaglandin D2 antagonist (fevipiprant)
- Antibiotics (macrolides), Antifungals
- TKA (masitinib), Antifibrotic drugs (rapamycin)
- Anti- IL-17, 33, 25.

# IL-5 as a therapeutic target in uncontrolled asthma with eosinophilic airway inflammation



**Mepolizumab for severe eosinophilic asthma (DREAM):  
a multicentre, double-blind, placebo-controlled trial**

Ian D Pavord, Stephanie Korn, Peter Howarth, Eugene R Bleecker, Roland Buhl, Oliver N Keene, Hector Ortega, Pascal Chanez

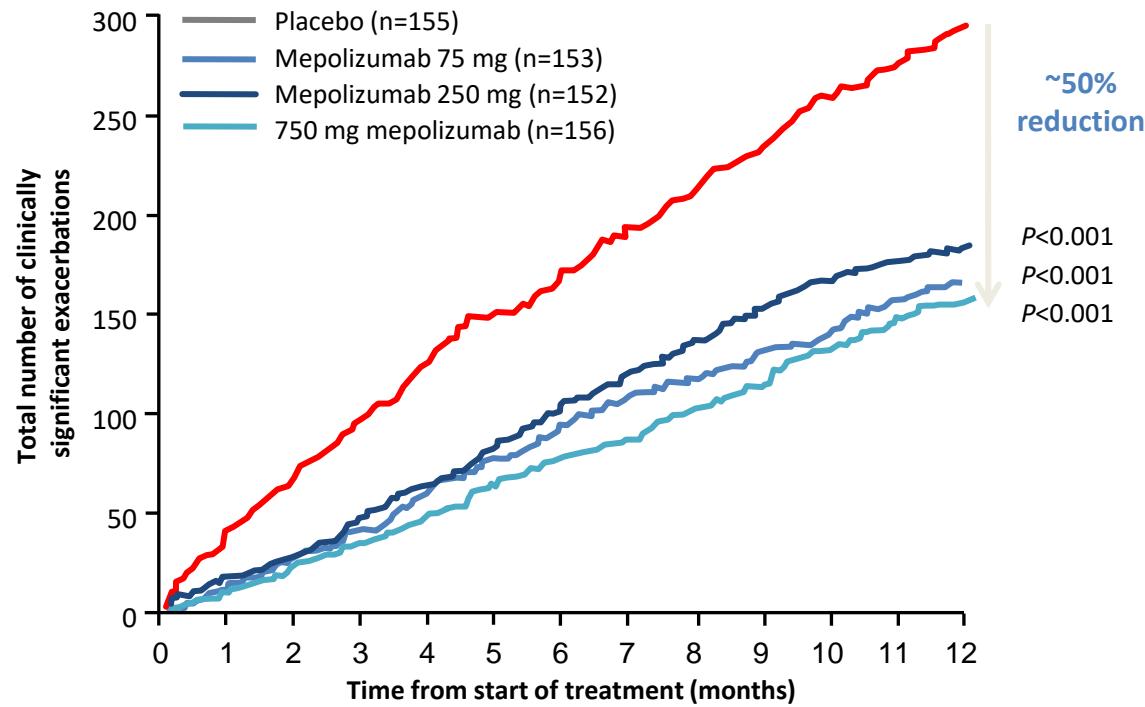
**Summary**

**Background** Some patients with severe asthma have recurrent asthma exacerbations associated with eosinophilic



Lancet 2012; 380: 651-59

# Exacerbations

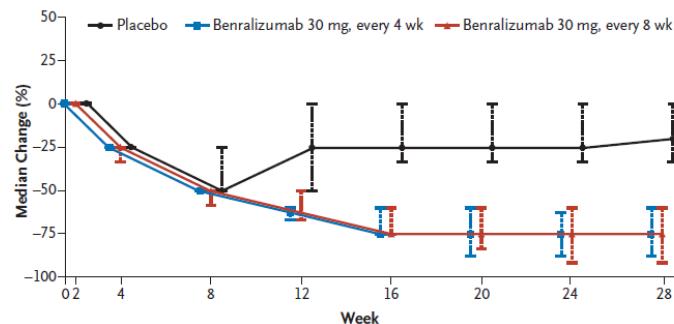


# Benralizumab - Zonda (Glucocorticoid dose)

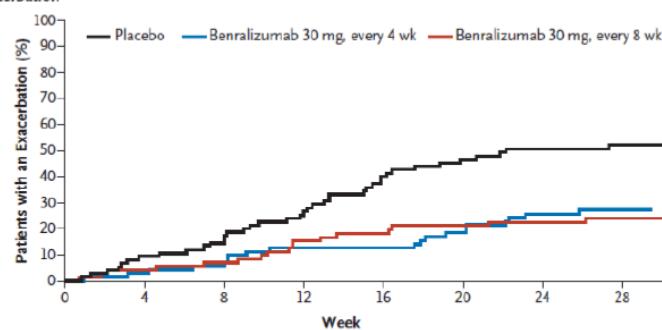
ORIGINAL ARTICLE

## Oral Glucocorticoid-Sparing Effect of Benralizumab in Severe Asthma

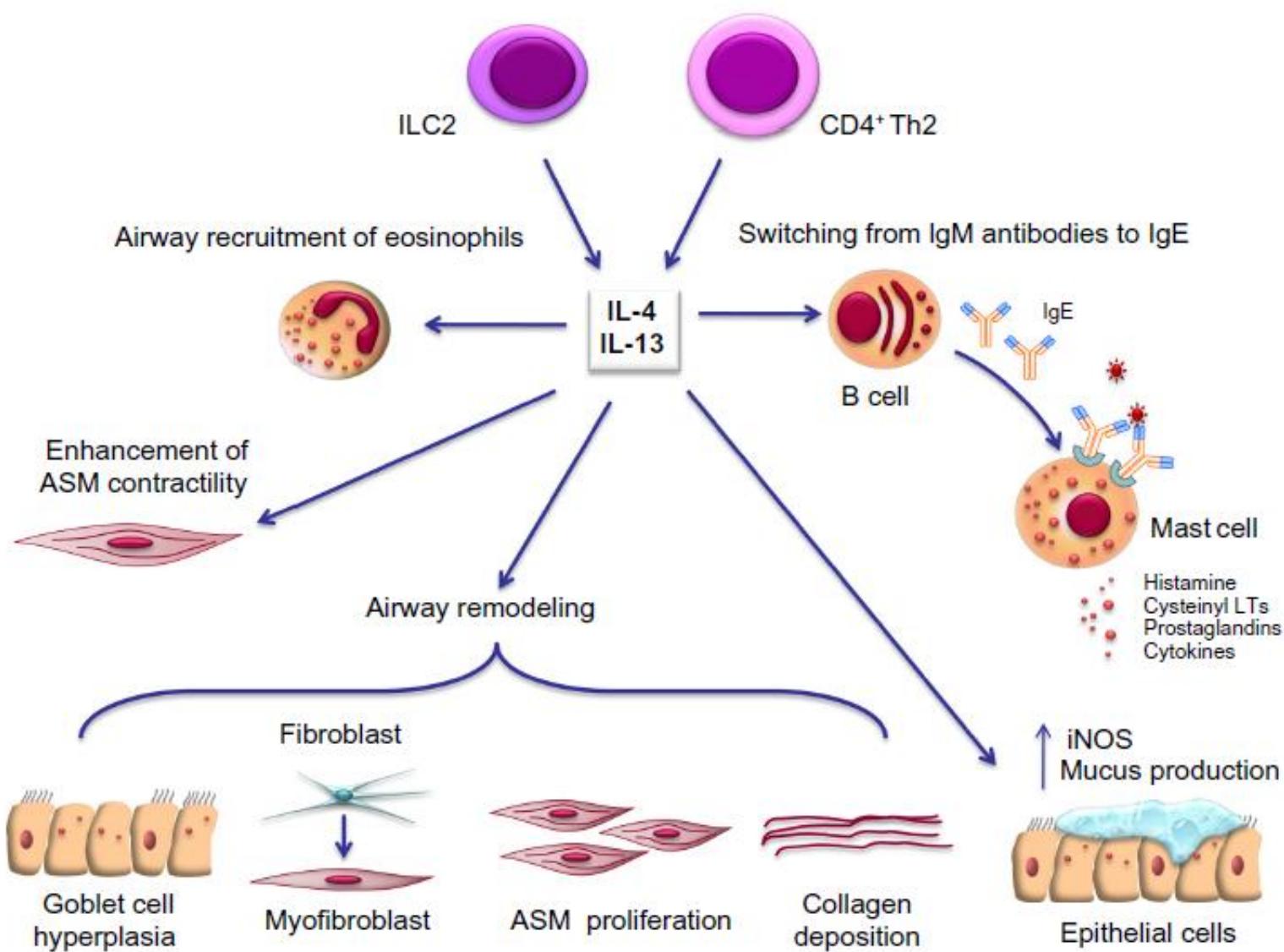
Parameswaran Nair, M.D., Ph.D., Sally Wenzel, M.D., Klaus F. Rabe, M.D., Ph.D., Arnaud Bourdin, M.D., Ph.D., Njira L. Lugogo, M.D., Piotr Kuna, M.D., Ph.D., Peter Barker, Ph.D., Stephanie Sproule, M.Math., Sandhia Ponnarambil, M.D., and Mitchell Goldman, M.D., for the ZONDA Trial Investigators\*

**A Change from Baseline in Oral Glucocorticoid Dose****No. at Risk**

Benralizumab 30 mg, every 4 wk	72	70	70	69	69	68	66	68
Benralizumab 30 mg, every 8 wk	70	72	67	69	69	66	69	68
Placebo	74	75	73	74	74	73	73	72

**B Time to First Asthma Exacerbation****No. at Risk**

Benralizumab 30 mg, every 4 wk	72	69	67	62	61	56	51	45
Benralizumab 30 mg, every 8 wk	73	68	66	60	58	56	55	51
Placebo	75	68	64	56	45	40	37	31

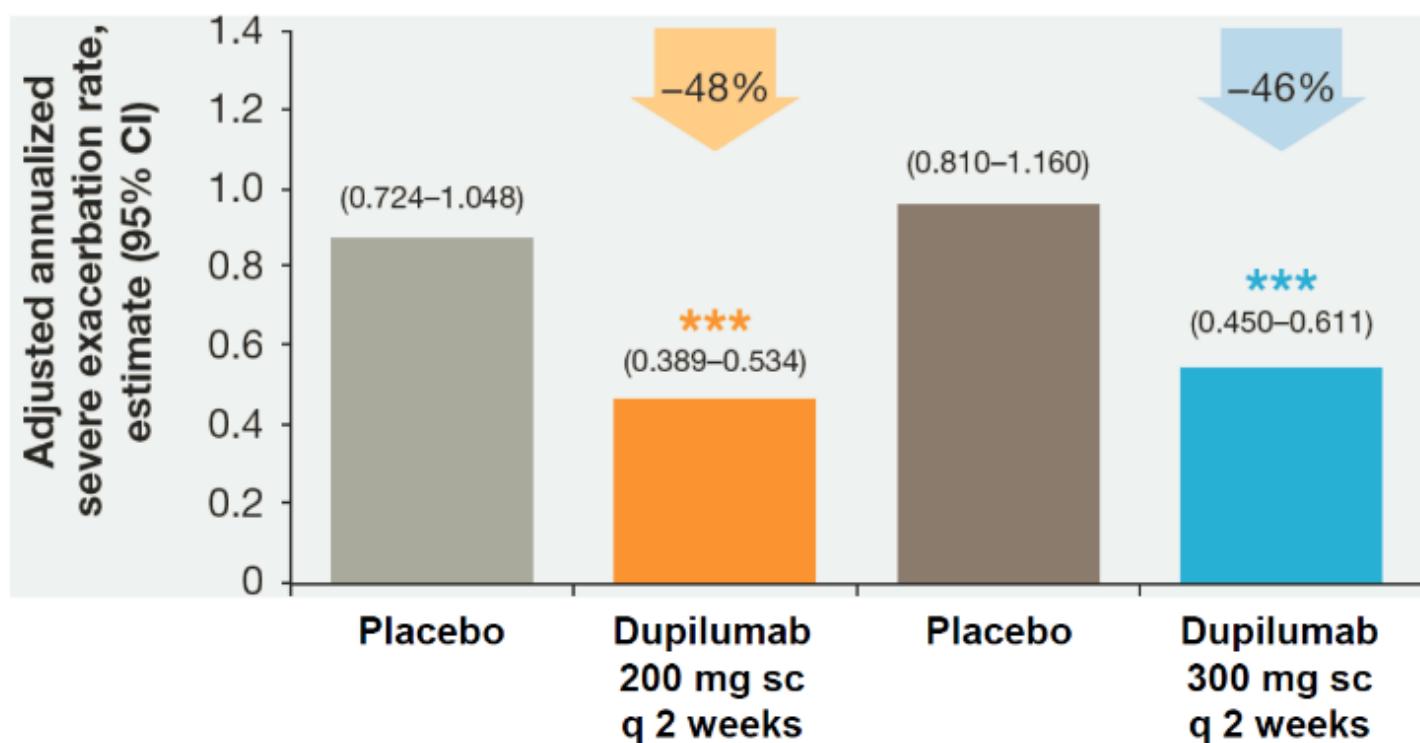


## Dupilumab Efficacy and Safety in Moderate-to-Severe Uncontrolled Asthma

M. Castro, J. Corren, I.D. Pavord, J. Maspero, S. Wenzel, K.F. Rabe, W.W. Busse, L. Ford, L. Sher, J.M. FitzGerald, C. Katelaris, Y. Tohda, B. Zhang, H. Staudinger, G. Pirozzi, N. Amin, M. Ruddy, B. Akinlade, A. Khan, J. Chao, R. Martincova, N.M.H. Graham, J.D. Hamilton, B.N. Swanson, N. Stahl, G.D. Yancopoulos, and A. Teper

# Dupilumab in uncontrolled moderate-to-severe asthma (LIBERTY ASTHMA QUEST)

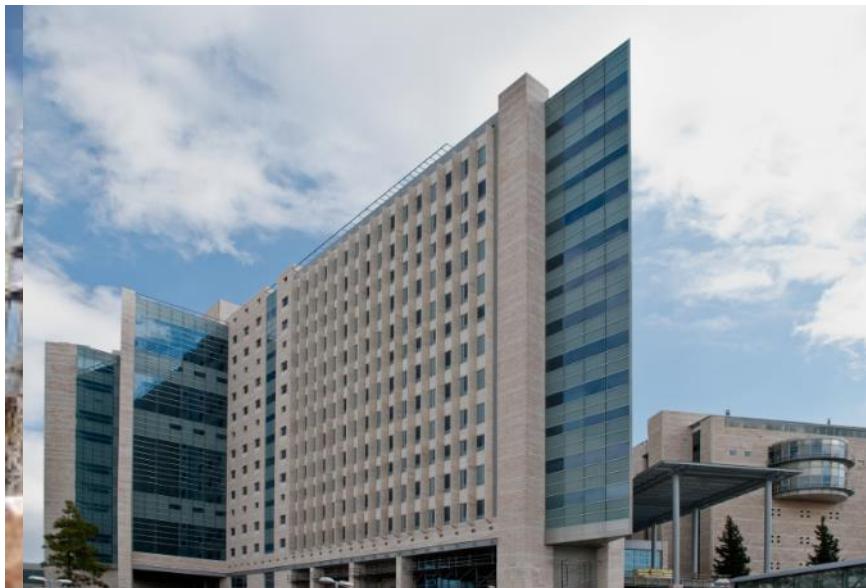
### Exacerbations [/year]



אֵה חַדְרָה כִּי־וְתִּחְנֹן  
? (ILD) יְסִיבַּת (ILD) יְסִיבַּת

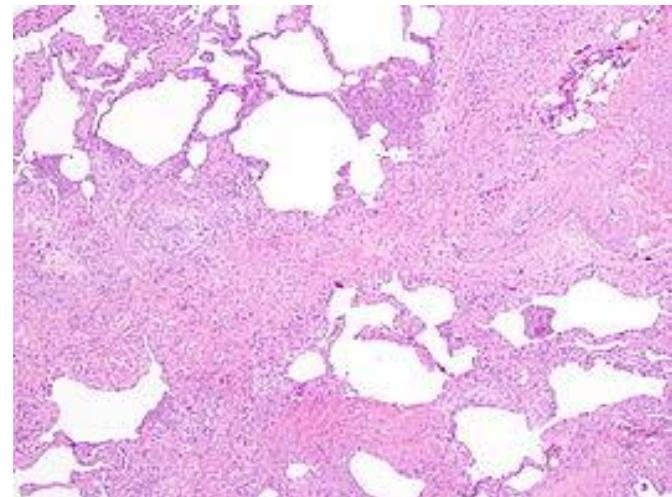
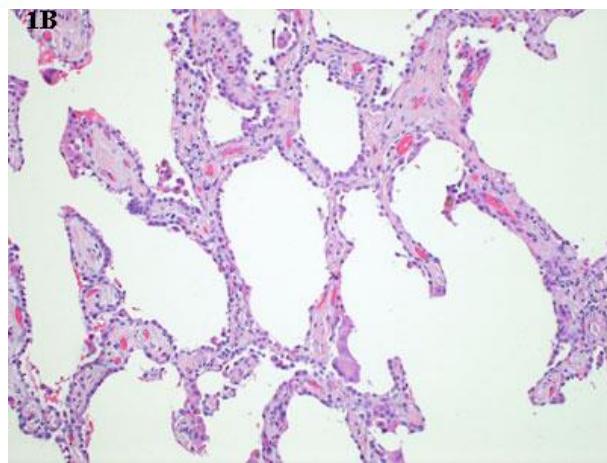
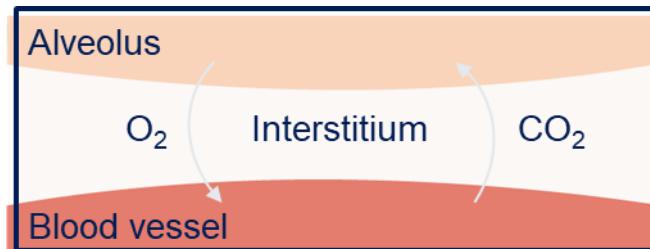
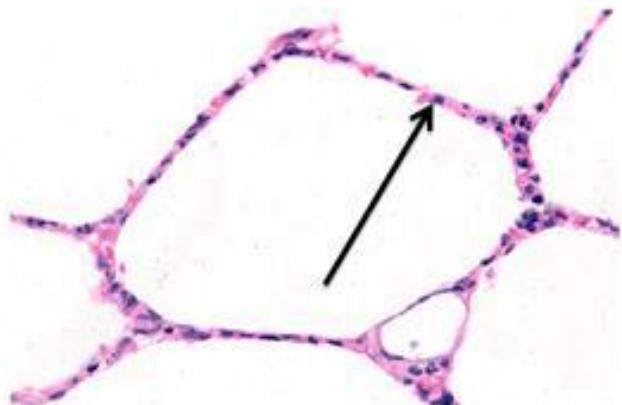


הקיירוסים



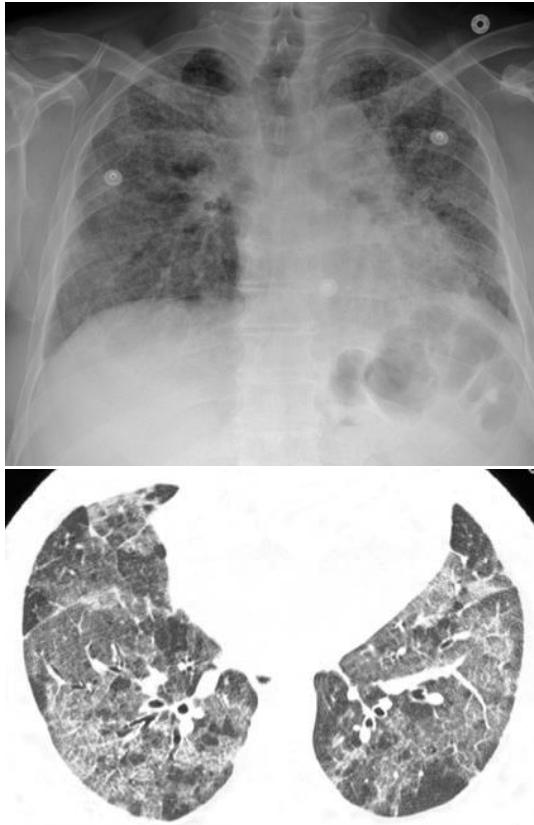
# אנטינט ריאתית

## היפרkapסיאציה



# אַמְגָוֶת רִיאָה קְיֻרְבָּנָסִיָּה

## Interstitial Lung Diseases (ILD)



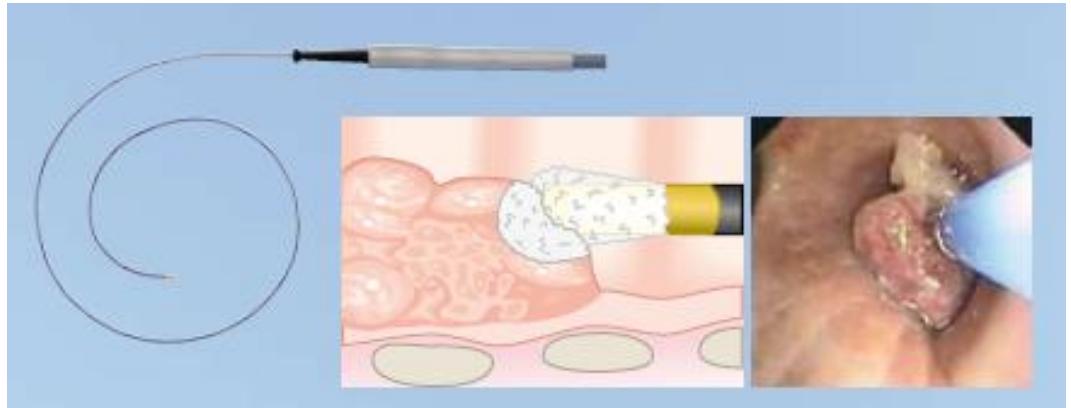
- קבוצה של יותר מ-200 (!) מחלות חריפות וכרוניות עם מידת משתנה של **דלקת ופיברוזיס** ריאתית.
- למעשה השם אינו מתאים ("Misnomer") –
  - המחלות מעורבות מרכיבים **תאיים** **ואינטראSTITיציאליים** של דופן האלבאולים (מעבר לחלל).
  - לכן מכונות לעיתים –
- Diffuse Parenchymal Lung Diseases
- מגוון גורמים טיפולים ופרוגנוזות

# Cryobiopsy



Sekil 1. Kriyo Cihazı

- ברונקוסkop המוביל את הcenתרא.
  - צנתר.
  - חומר מkapיא – חנקן נוזלי.
- 
- הרקמה מוקפאת לטמפרטורה של  $20^{\circ}\text{C}$ - $40^{\circ}\text{C}$  - .



# Fibrosing Progressive ILD & Connective tissue disease associated ILD (CT-ILD) -

חיזואיד מחלת גאנגרה וגד'ריה



# אלהמת רקamt מהימן

## אלהמת סטת הילא

מעורבות ריאתית קיימת במעלה 25%  
מקרים מחלות רקמת חיבור

**Table 1. Interstitial lung diseases associated with connective tissue diseases**

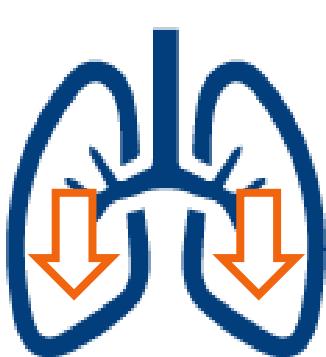
Rheumatic disease	Frequency of ILD (%)
Systemic sclerosis	45 (clinically significant)
Rheumatoid arthritis	20 to 30
Polymyositis/dermatomyositis	20 to 50 <sup>a</sup>
Sjögren's syndrome	Up to 25
Systemic lupus erythematosus	2 to 8
Mixed connective tissue disease	20 to 60

אלהמת קיפל אלהמת סטת הילא  
 מתזיכת פגעה, וככיהות אהוות שוקן נסכך  
 נסכך המהמפה והמתואמת לה.

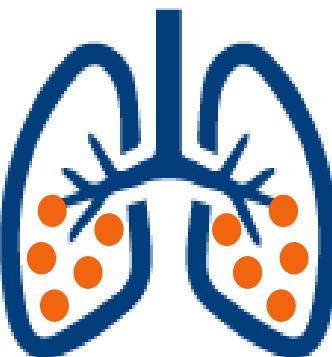
# Today an entity called Progressive fibrosing ILDs is recognized

Patients with **chronic fibrosing ILDs** other than IPF are at risk of developing a **progressive phenotype**.

The natural history of progressive fibrosing ILDs, as with IPF, is characterized by:



Decline in  
lung function



Increase in  
fibrosis



Worsening symptoms  
and QoL



Early mortality

As many as 18% to 32% of patients with non-IPF ILDs are estimated to be at risk of developing a progressive fibrosing phenotype<sup>1</sup>

ORIGINAL ARTICLE

## Nintedanib in Progressive Fibrosing Interstitial Lung Diseases

K.R. Flaherty, A.U. Wells, V. Cottin, A. Devaraj, S.L.F. Walsh, Y. Inoue, L. Richeldi,  
M. Kolb, K. Tetzlaff, S. Stowasser, C. Coeck, E. Clerisme-Beaty, B. Rosenstock,  
M. Quaresma, T. Haeufel, R.-G. Goeldner, R. Schlenker-Herceg, and K.K. Brown,  
for the INBUILD Trial Investigators\*

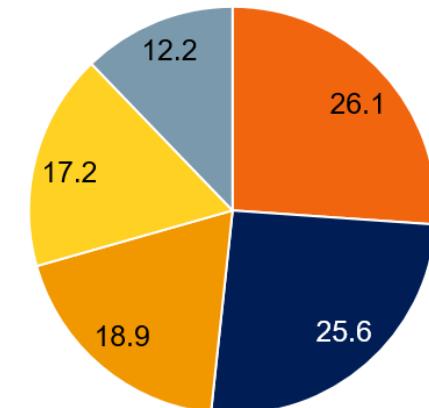
## INBUILD Trial - ILD Subgroups

### *ILD diagnoses documented on case report form*

- iNSIP
- Unclassifiable IIP
- Hypersensitivity pneumonitis
- RA-ILD
- SSc-ILD
- MCTD-ILD
- Exposure-related ILD
- Sarcoidosis
- Other fibrosing ILD (specified in text box)



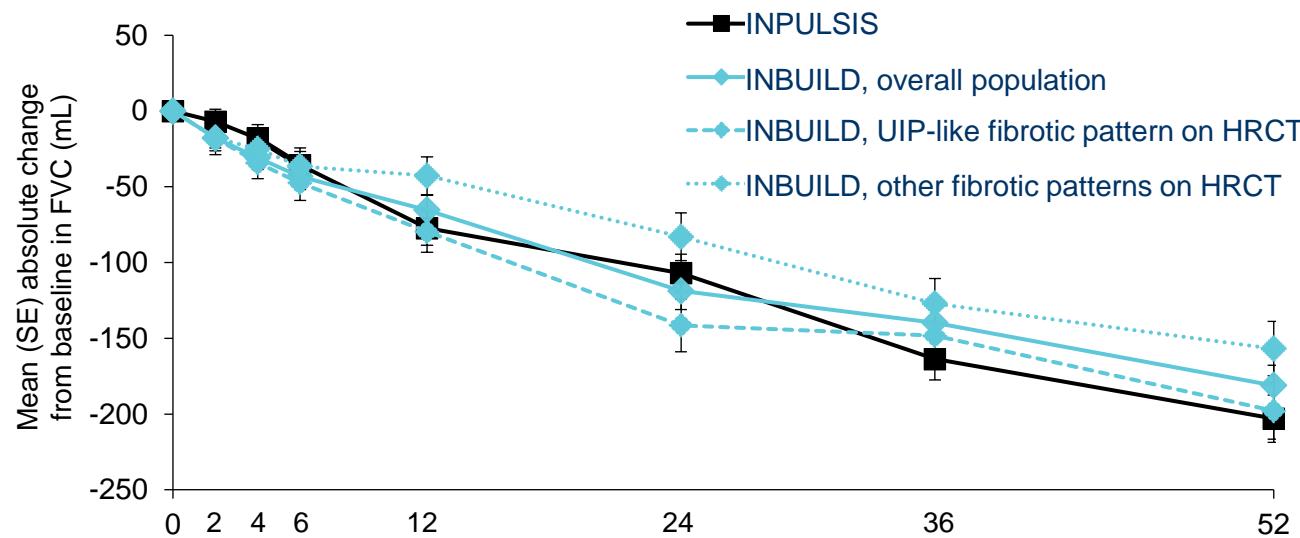
### *ILD diagnoses in 5 groups in*



- Hypersensitivity pneumonitis
- Autoimmune ILDs
- iNSIP
- Unclassifiable IIP
- Other ILDs

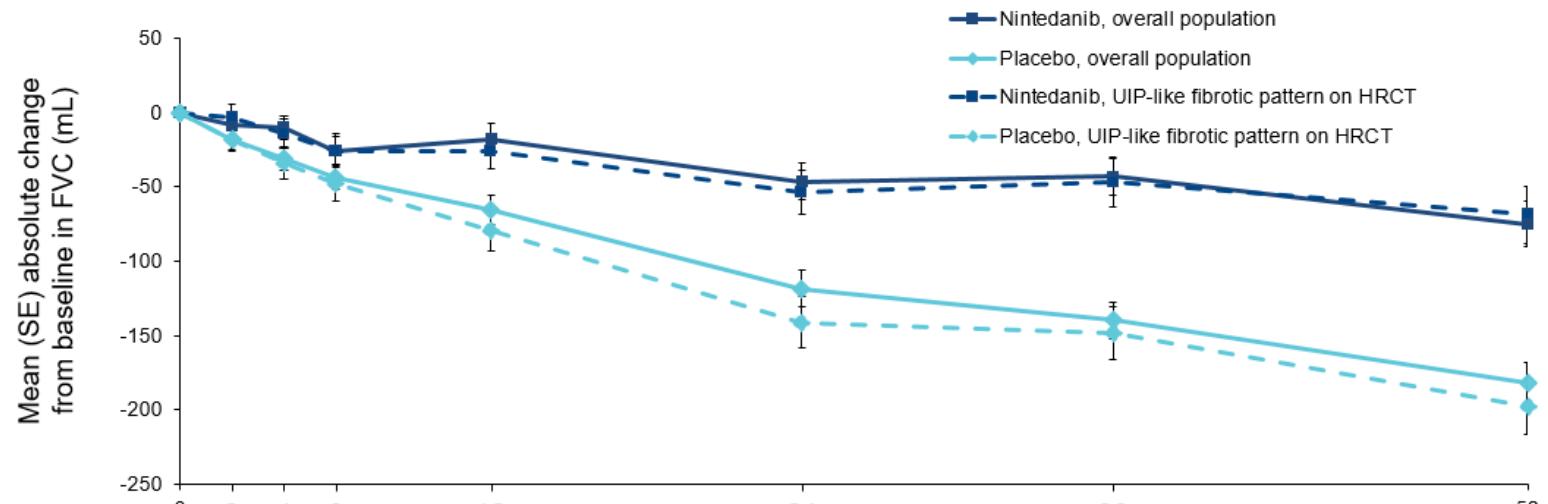
# Progressive fibrosing ILDs, as defined in the Phase III INBUILD trial, share a similar disease course to IPF<sup>1</sup>

Annual rate of decline in FVC (mL/year) over 52 weeks in the placebo groups of the INBUILD and INPULSIS trials<sup>2</sup>



Progressive fibrosing ILDs  
share a **similar**  
**pathophysiology** with that  
of IPF<sup>2,3</sup>

# Observed change from baseline in FVC (mL) over 52 weeks



## No. of patients Overall population

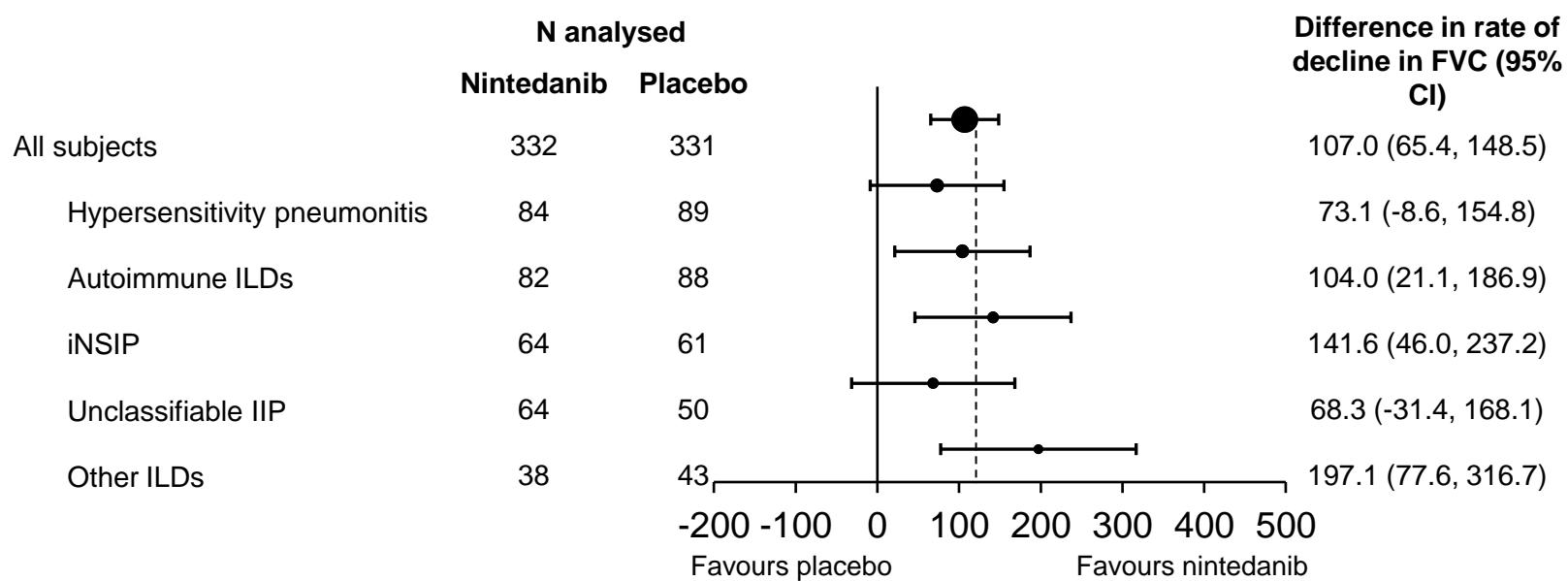
Nintedanib	332	326	320	322	314	298	285	265
Placebo	331	325	326	325	320	311	296	274

## UIP-like fibrotic pattern on HRCT

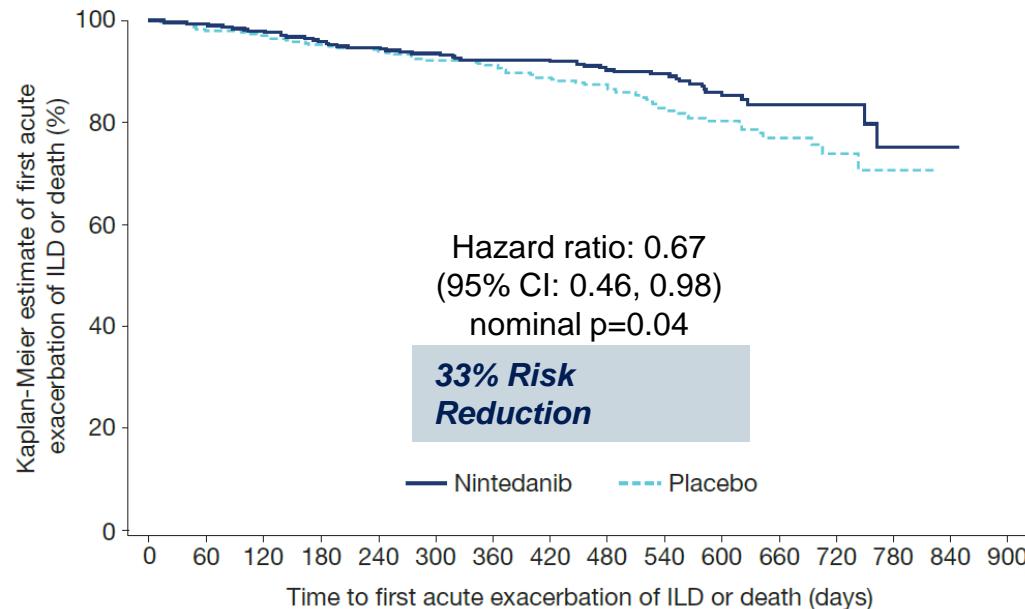
Nintedanib	206	203	200	199	193	180	171	160
Placebo	206	202	202	201	197	190	176	162

**Nintedanib demonstrates Early and sustained reduction in FVC through 52 weeks**

# INBUILD: Rate of decline in FVC (mL/year) over 52 weeks with nintedanib vs placebo by ILD diagnosis in the overall population



# Time to first acute exacerbation of ILD or death in overall population over the whole trial



**n (%) with event:**

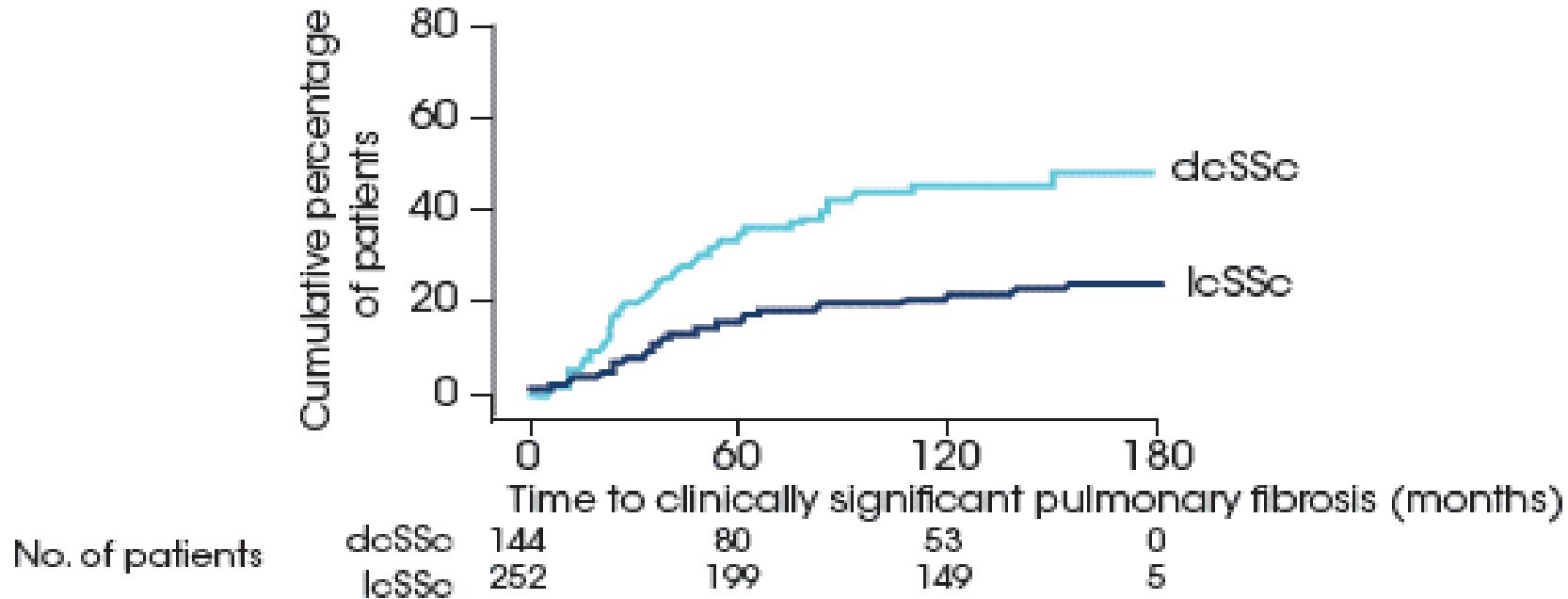
Nintedanib: 46 (13.9%)

Placebo: 65 (19.6%)

וַיְכִלֵּם קָרְבָּן – כִּימְלָאָה,  
מִתְּחִילָה, סַדְּגָרָה וְעַצְמָה

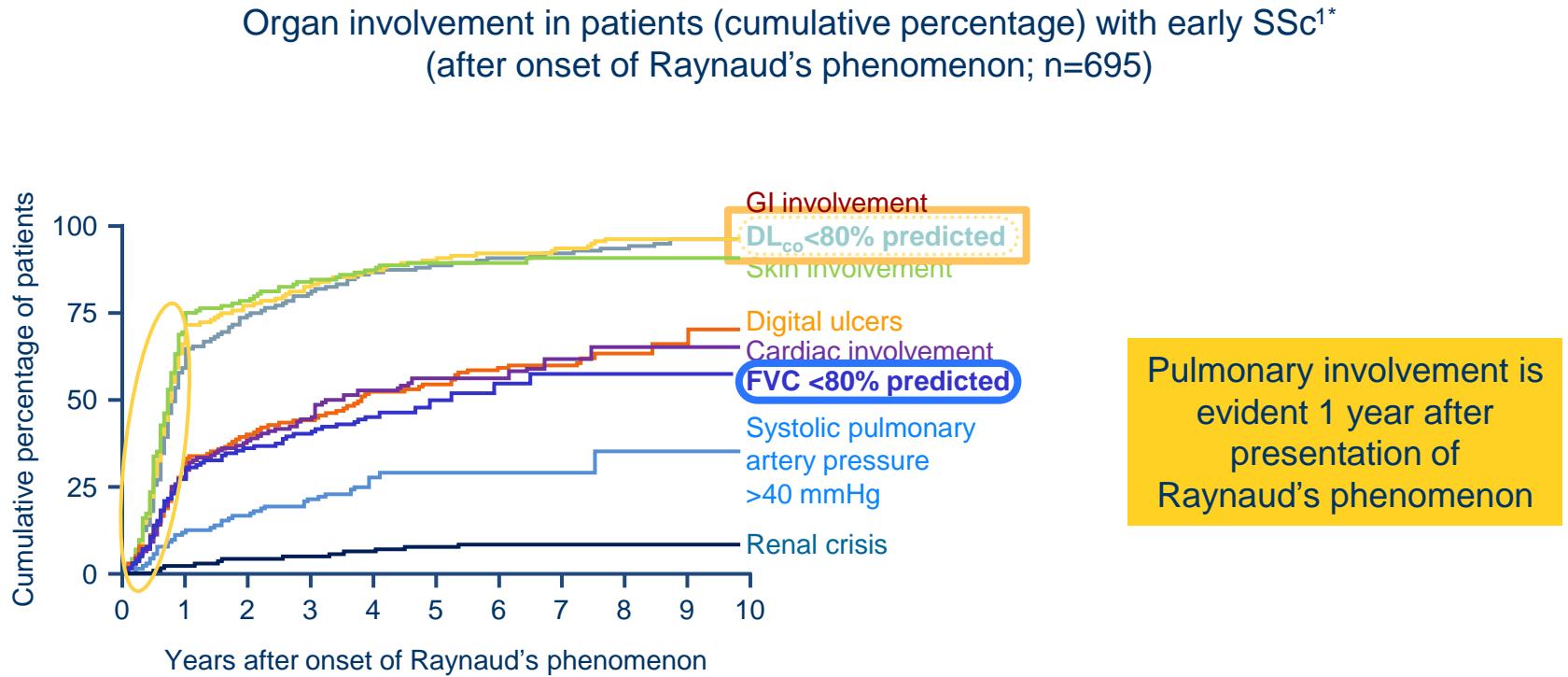


# ILD is a Common Manifestation in Diffuse but also in Limited Cutaneous SSc Subsets



Mean disease duration at time of first assessment was 18 (95% CI 16–20) months in patients with dcSSc and 31 (95% CI 27–36) months in patients with lcSSc.

# ILD develops early in the disease course of SSc



\*Skin involvement was defined as modified Rodnan skin score of ≥2 at any part of the body; cardiac involvement was defined as the presence of diastolic dysfunction, conduction blocks, left ventricular ejection fraction <50% or a pericardial effusion; systolic pulmonary artery pressure was estimated by echocardiography

1. Jaeger VK et al. PLoS One 2016;11:e0163894

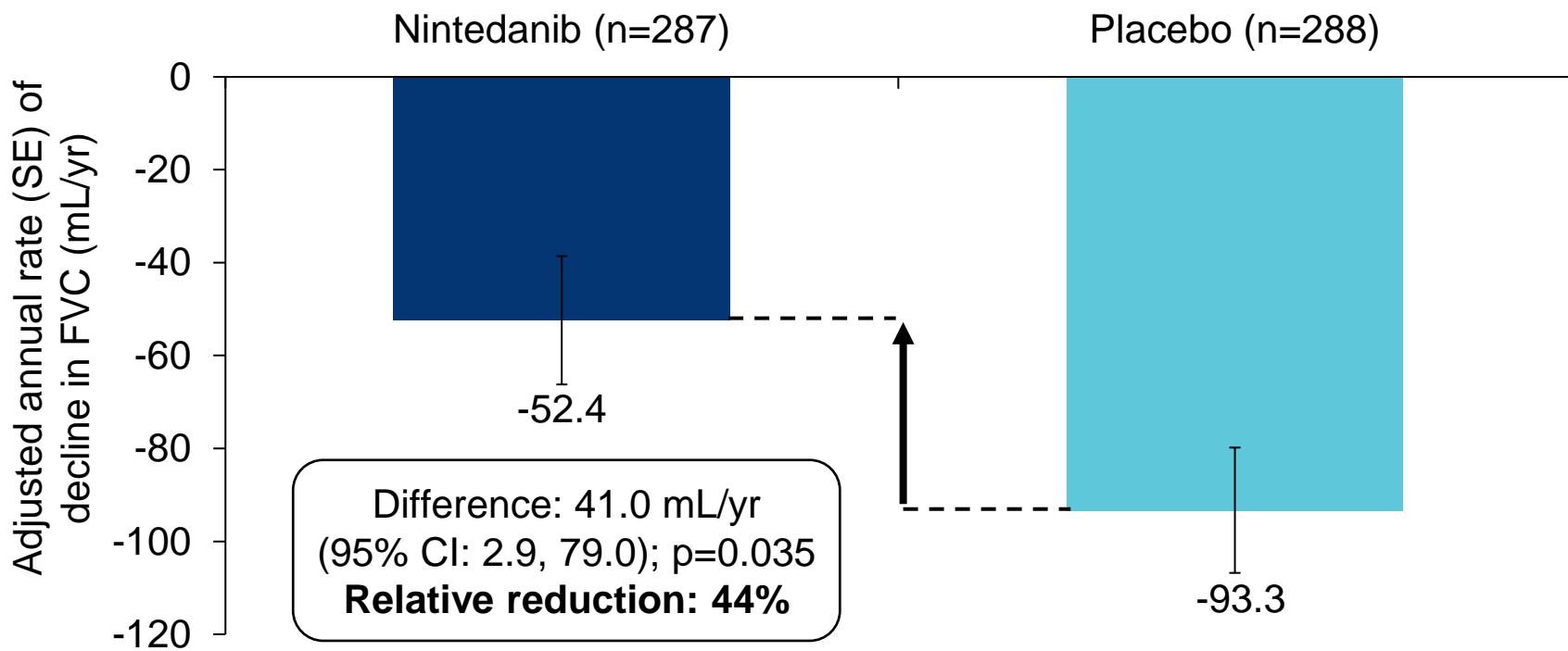


ORIGINAL ARTICLE

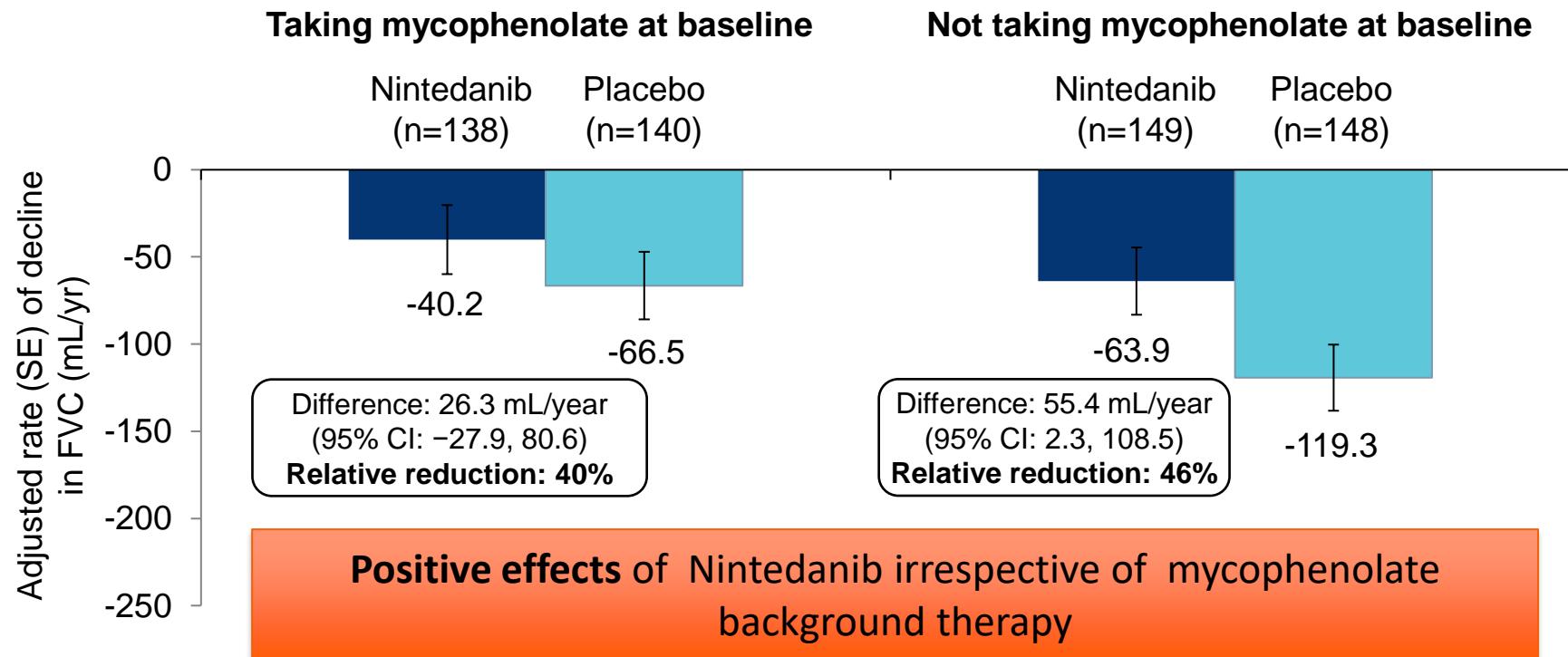
Nintedanib for Systemic Sclerosis–  
Associated Interstitial Lung Disease

Oliver Distler, M.D., Kristin B. Highland, M.D., Martina Gahlemann, M.D.,  
Arata Azuma, M.D., Aryeh Fischer, M.D., Maureen D. Mayes, M.D.,  
Ganesh Raghu, M.D., Wiebke Sauter, Ph.D., Mannaiq Girard, M.Sc.,  
Margarida Alves, M.D., Emmanuelle Clerisme-Beaty, M.D.,  
Susanne Stowasser, M.D., Kay Tetzlaff, M.D., Masataka Kuwana, M.D.,  
and Toby M. Maher, M.D., for the SENSCIS Trial Investigators\*

## SENSCIS: Annual Rate of Decline in FVC (mL/yr) Over 52 Weeks (Primary Endpoint)



# Rate of Decline in FVC (mL/yr) Over 52 Weeks by Mycophenolate Use at Baseline



?COPD-ג אָמֵן נַחַת



# Annual Decline in Post-Bronchodilator FEV1 in Major COPD Clinical Trials

Study	Treatment	Treatment (mL/year)	Placebo (mL/year)
EUROSCOP (1992)	Budesonide	57	69
ISOLDE	Fluticasone	50	59
LHS II	Triamcinolone	44	47
BRONCUS	NAC	56	47
TORCH	S/F/SFC	39-42	55
UPLIFT	Tiotropium	37	42
SUMMIT (2016)	Seretide	38	46

\*3 year trials

# משאיפים לטיפול במערכת הנשימה במוגרים

## MDI

שאף דוד אינהילר TITTO

**Ventolin®**  
(*Salbutamol*)  
Use: 2-8 puffs/day PRN  
Strength: 100 mcg  
(GlaxoSmithKline)

**Atrone®**  
(*Ipratropium*)  
Use: 2-8 puffs/day PRN  
Strength: 20 mcg  
(Boehringer Ingelheim)

**Serevent®**  
(*Salmeterol*)  
Use: BID  
Strength: 25 mcg  
(GlaxoSmithKline)

**Qvar®**  
(*Bclometasone*)  
Use: BID  
Strength: 50, 100 mcg  
(Teva)

**Qvar® Autohaler®**  
(*Bclometasone*)  
Use: 100-400 mcg OD or BID  
Strength: 50, 100 mcg  
(Teva)

**Flixotide® Inhaler®**  
(*Fluticasone propionate*)  
Use: 100-1000 mcg BID  
Strength: 50\*, 125\*, 250 mcg  
(GlaxoSmithKline)

**Foster® 100/6, Foster® 200/6+**  
(*Bclometasone dipropionate/Formoterol*)  
Use: BID  
Strength: 100/6, 200/6+ mcg  
(Kamada)

**Flutiform®**  
(*Fluticasone propionate/Formoterol*)  
Use: BID  
Strength: 50/5, 125/5, 250/10 mcg  
(Rafa)

## DPI

שאפי אבקה יבשה

**Ventolin® Diskus®**  
(*Salbutamol*)  
Use: 1-4 puffs/day PRN  
Strength: 200 mcg  
(GlaxoSmithKline)

**Serevent® Diskus®**  
(*Salmeterol*)  
Use: BID  
Strength: 50 mcg  
(GlaxoSmithKline)

**Flixotide® Diskus®**  
(*Fluticasone propionate*)  
Use: 100-1000 mcg BID  
Strength: 50\*, 100\*, 250, 500 mcg  
(GlaxoSmithKline)

**Seretide® Diskus®**  
(*Fluticasone propionate/Salmeterol*)  
Use: BID  
Strengths: 100/50\*, 250/50, 500/50 mcg  
(GlaxoSmithKline)

**Relvar® Ellipta®**  
(*Fluticasone Furoate/Vilanterol*)  
Use: OD  
Strength: 92/22, 184/22\* mcg  
(GlaxoSmithKline)

**Incruse® Ellipta®**  
(*Umeclidinium*)  
Use: OD  
Strength: 55 mcg  
(GlaxoSmithKline)

**Anoro™ Ellipta®**  
(*Umeclidinium/Vilanterol*)  
Use: OD  
Strength: 55/22 mcg  
(GlaxoSmithKline)

**Trelegy Ellipta**  
(*Fluticasone Furoate/Umeclidinium/Vilanterol*)  
Use: OD  
Strength: 92/55/25 mcg  
(GlaxoSmithKline)

## SMI

שאף מים לשאייה

**Spiriva® Respimat®**  
(*Tiotropium*)  
Use: 2 actuations OD  
Strength: 2.5 mcg/actuation  
(Boehringer Ingelheim)

**Pioltol® Respimat®**  
(*Tiotropium/Olodaterol*)  
Use: 2 actuations OD  
Strength: 2.5/2.5 mcg/actuation  
(Boehringer Ingelheim)

1. השוואת שיטות כלולות לטשפאים:
2. השוואת עמידת היחסנות סיד אחדו השטיפה
3. יש להזכיר לברור את השראף עם המכסה
4. במום חסרון - ניתן כוונת תקיקת
5. ניר טיפות - יבצע עם סולית או ניר טיפות יבשין

## הנחיות הטיפול והمتابعة במשאיפים

### ברור

- ברור טיפאי סטטוס בעקבות תוצאות הבדיקה הדרושים לפיה:
- אכפוי סטטוס (אילו), קושי קבוצתי או אישי, חזרה או עתודה.
- ממליל לברר ולטפל בשטרס סטטוס (autohaler).
- אם רגש רותם מושך אויך, רצוי להשתמש באותו סטטוס שטאו, בסיום, בסיום האפשר.

### בודק

- בדק אוק סכינית השירות בסחף בכל גודלנות:
- "הוא תכליל" יהודים לא את השירות בסחף של ?"

### תקין

- מון לאירועי גירוי טעימות.
- בדק את הדגמה חותמת בכנה ע"י הסופג
- (סומסן 2-3 פעימות).

### דוח

- ווא שיטוט סטטוס במשאיף כבושא של 4-6 שניות.
- סוחלת הפעישות בסחף.
- ווא שיטוט לטעמך: כהה פגסם בשבעו אתה שטוטש בסחף של ?"

## אופן השטיפה במשאיפים השונים

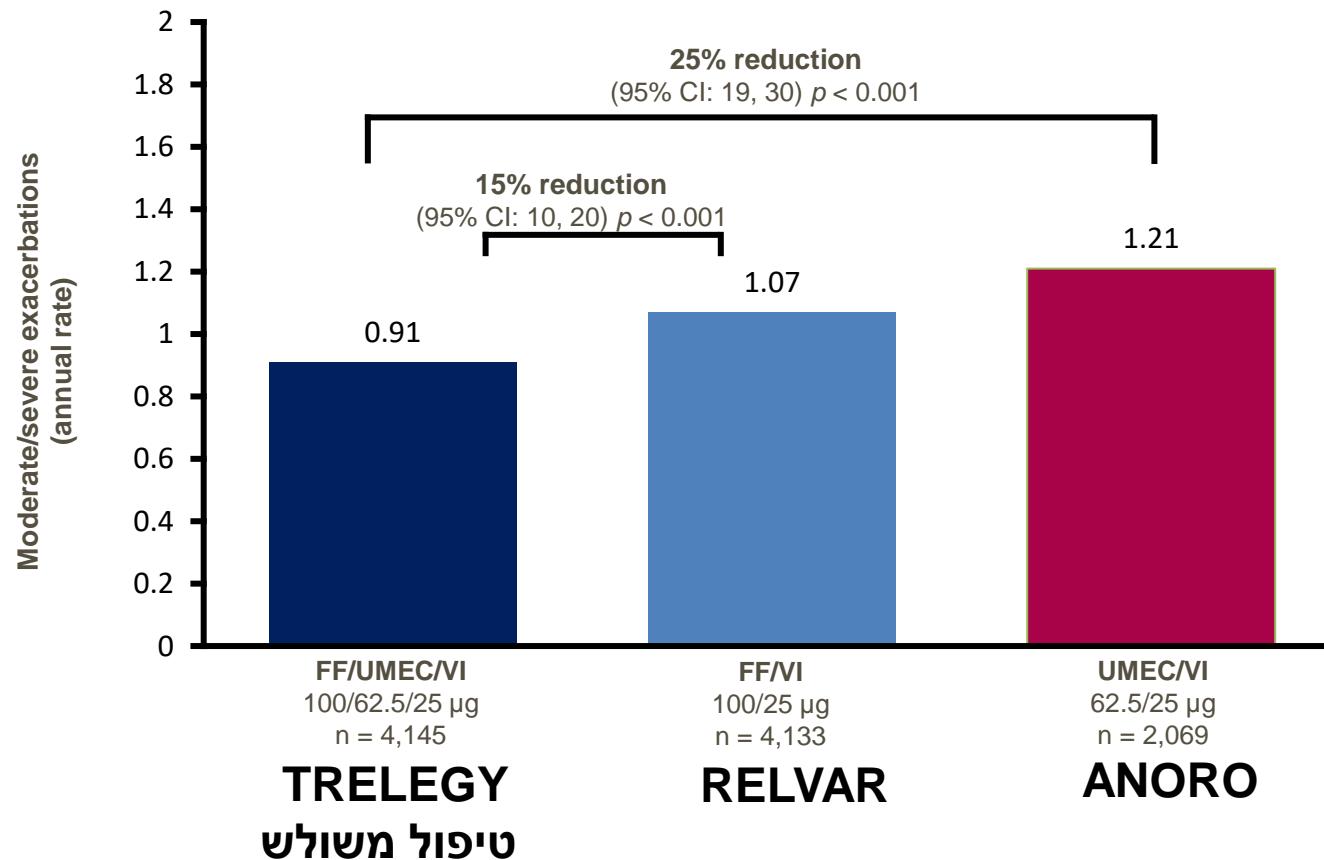
משאיף + MDI: שטיפה נזקקה, אסידית ומוסחת (5 פעימות)

משאיף SMI: שטיפה נזקקה כבושא של 2-5 פעימות

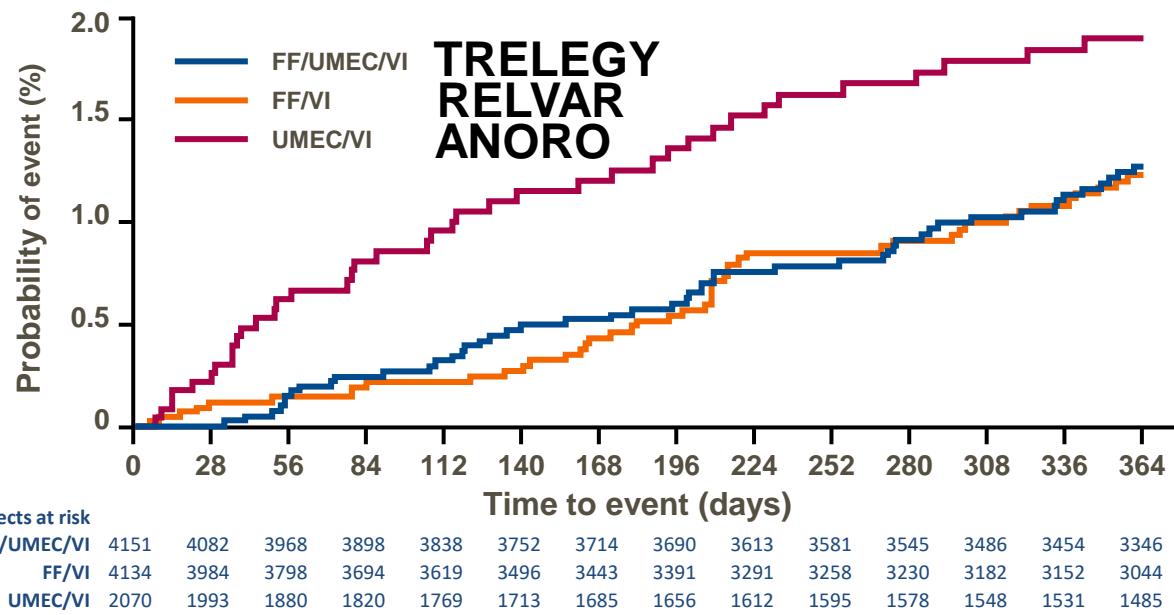
משאיף DPI: שטיפה נזקקה כבושא של 2 פעימות

# Significant reduction in moderate/severe exacerbations with FF/UMECA/VI (LABA+LAMA+ICS) vs FF/VI and UMEC/VI

## IMPACT TRIAL



# *Significant reduction in the risk of all-cause mortality with FF-containing treatment vs UMEC/VI*



Relative risk reduction:  
FF/UMEV/VI vs  
UMEV/VI

**42.1%**

HR 0.58  
(95% CI: 0.38, 0.88)  
p=0.011

FF/VI vs UMEV/VI

**38.7%**

HR 0.61  
(95% CI: 0.40, 0.93)  
p=0.022

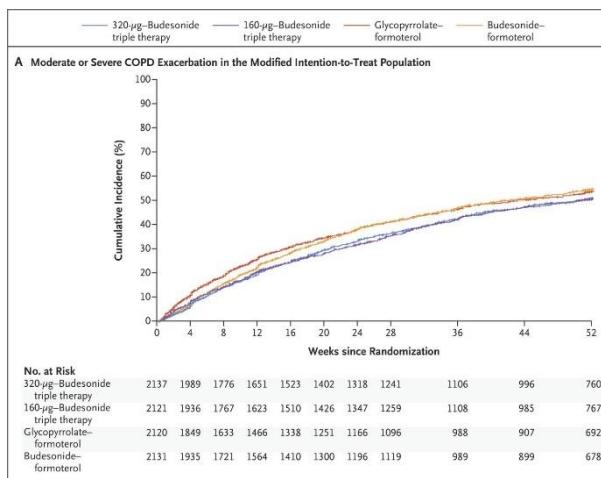
IMPACT is the first study with prospective data showing a reduction in the risk of all cause mortality with a COPD medication

# ETHOS study

## Results: Moderate/severe exacerbations by prior triple therapy use

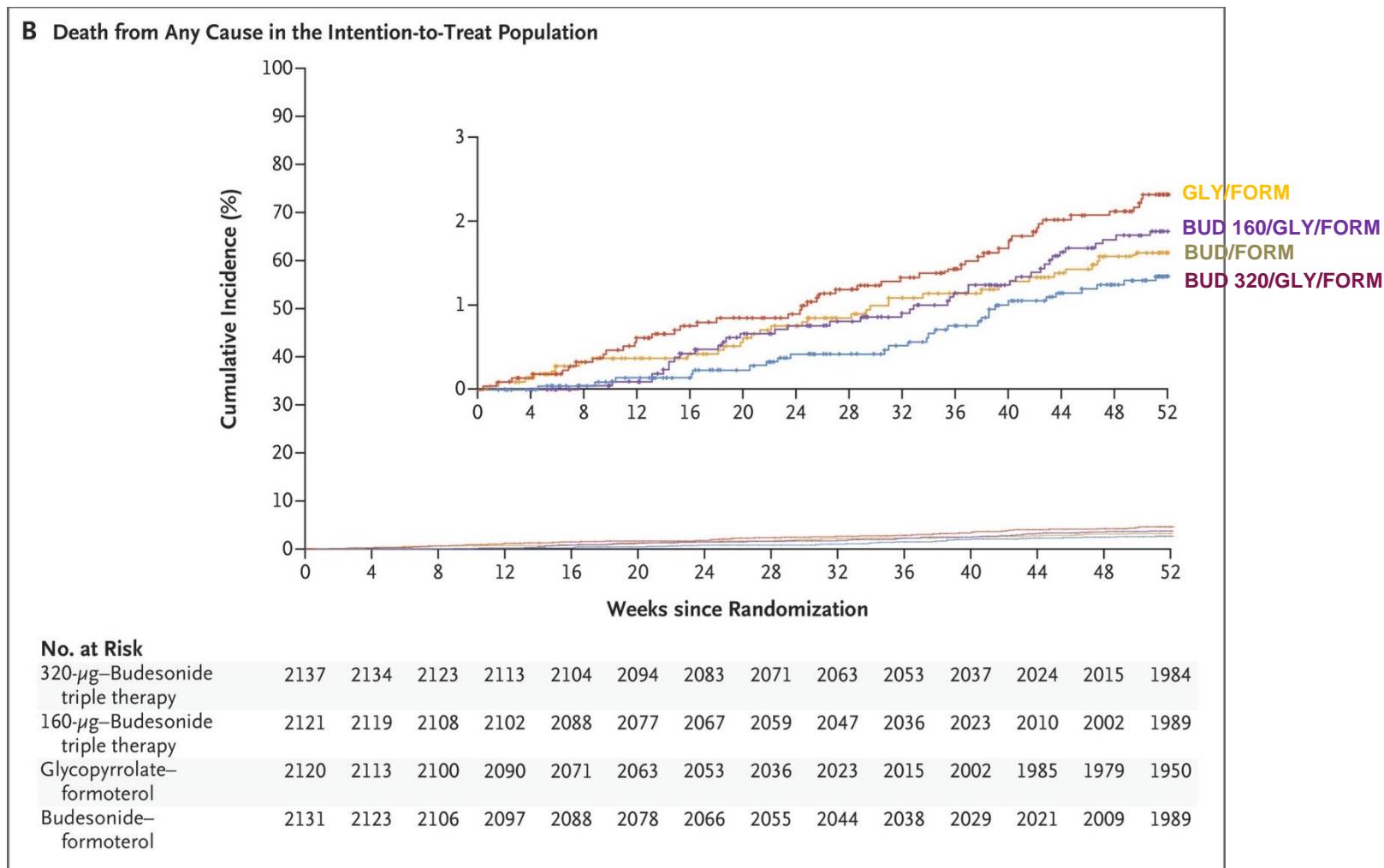
- The modified ITT population included 8509 patients
  - Prior triple therapy: N=3899 (45.8%)
  - No prior triple therapy: N=4610 (54.2%)
- Rates of moderate/severe exacerbations were lower with both doses of BGF compared with GFF in patients with and without prior triple therapy

	Prior triple therapy <sup>a</sup>			No prior triple therapy <sup>a</sup>		
	BGF 320/14.4/10 µg (N=983)	BGF 160/14.4/10 µg (N=991)	GFF 14.4/10 µg (N=979)	BGF 320/14.4/10 µg (N=1154)	BGF 160/14.4/10 µg (N=1130)	GFF 14.4/10 µg (N=1141)
Patients with moderate/severe exacerbations, n (%)	499 (50.8)	535 (54.0)	539 (55.1)	527 (45.7)	478 (42.3)	517 (45.3)
Model-adjusted rate per year of moderate/severe exacerbations	<b>1.23</b>	<b>1.31</b>	<b>1.78</b>	<b>0.96</b>	<b>0.88</b>	<b>1.16</b>



# ETHOS study - Results: Mortality

— 320- $\mu$ g-Budesonide triple therapy   — 160- $\mu$ g-Budesonide triple therapy   — Glycopyrrolate-formoterol   — Budesonide-formoterol



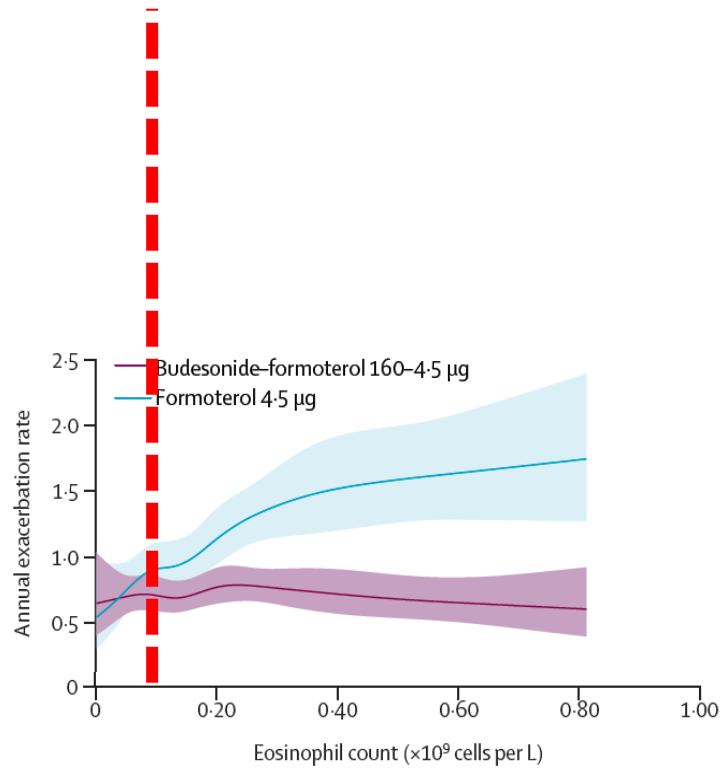
# Blood eosinophil count and outcomes

Data from 3 RC trials of:  
B/F versus F alone who  
had eosinophils measured

N = 4153 patients

FEV<sub>1</sub> = 1 L 38% pred

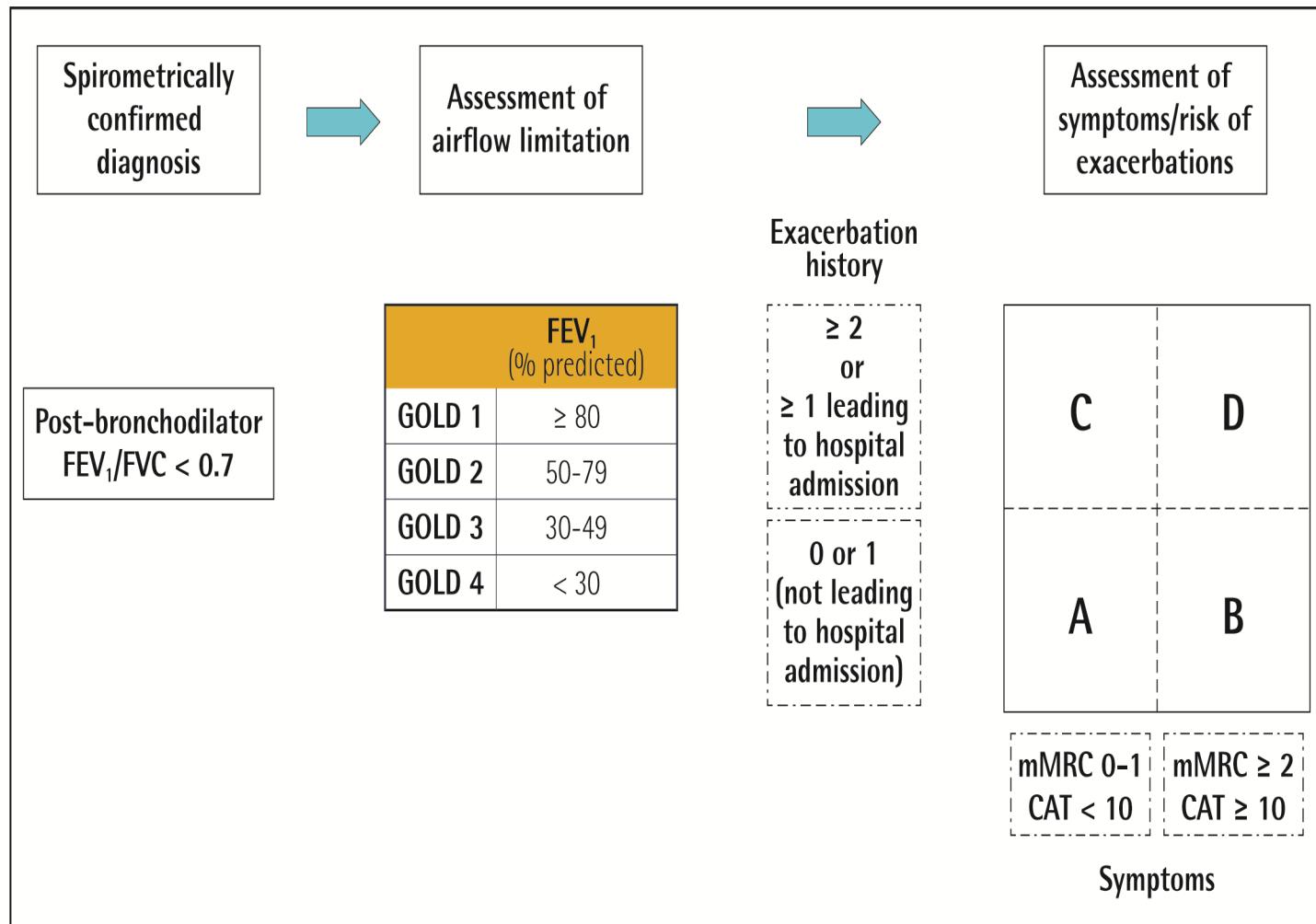
Outcomes:  
Exacerbations  
FEV<sub>1</sub>  
QoL



Bafadhel M et al Lancet RM 2018;6:117

# COPD diagnosis and classification

Figure 2.4. The refined ABCD assessment tool





# GOLD 2019

## stable COPD - Initiation

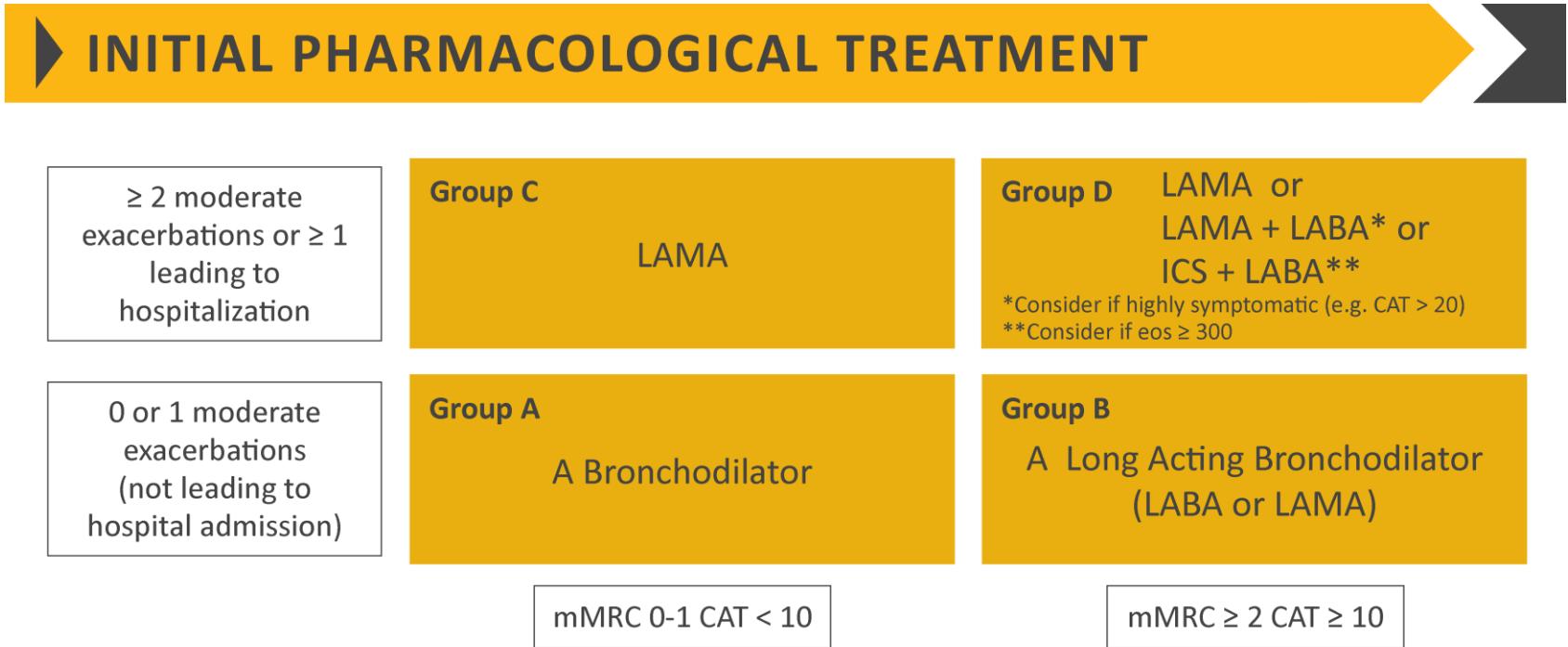
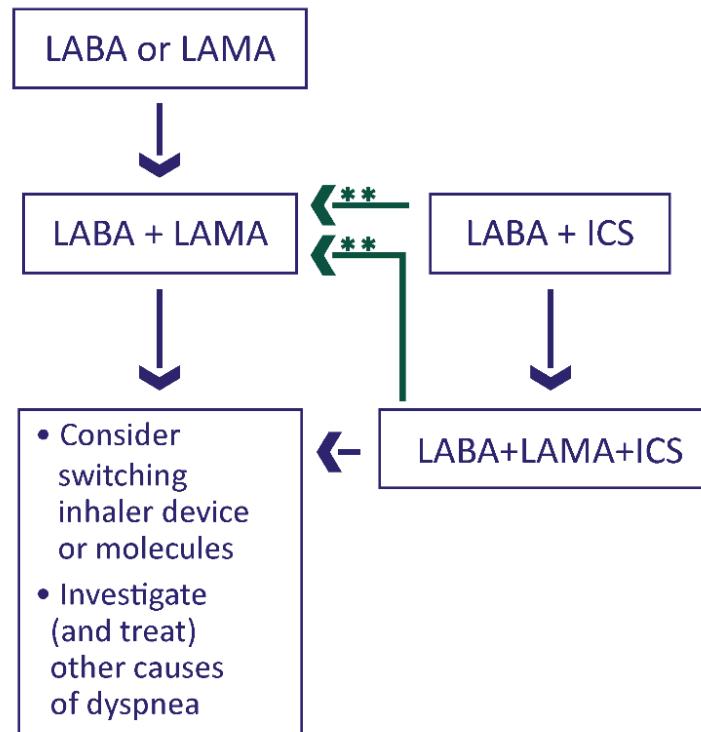


FIGURE 4.1

# GOLD 2020

## stable COPD – Follow up

### [Dyspnea]



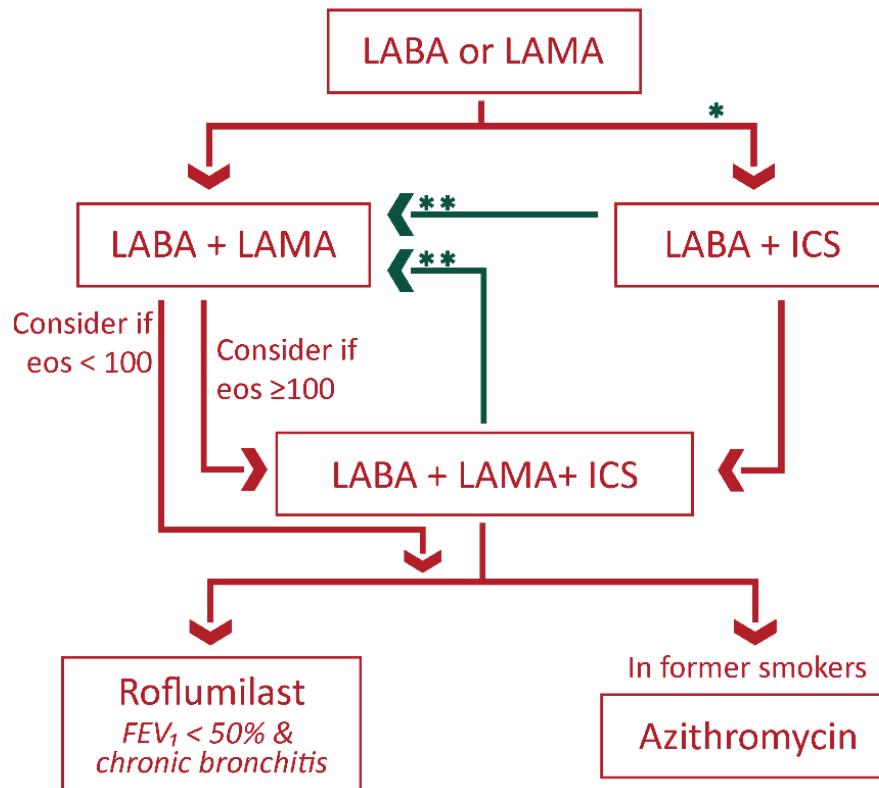
\*\* Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS



# GOLD 2020

## stable COPD – Follow up

### [Exacerbations]



\* Consider if eos  $\geq 300$  or eos  $\geq 100$  AND  $\geq 2$  moderate exacerbations / 1 hospitalization

\*\* Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS

**היא מחלת COPD  
ברט-אווירית  
ברט-ביצתית !!!**

ההזה גספירית נזקנית  
סיגריה? fe



## Early stage NSCLC > LDCT screening RCT [NELSON]

### NELSON

- Age 50-74
- Smoker/Ex-smoker\*
- No poor self-reported health (unable to climb 2 flights of stairs)
- Weight <140 kg
- Current or past cancer (lung, renal, breast, melanoma)
- Chest CT <1Y ago

\* >10/d for >30Y or >15/d for >25Y

\* smoking cessation <10Y

N=7900

R

N=7892

LDCT screening  
in year 1, 2, 4, 6.5

No screening

### Primary endpoint

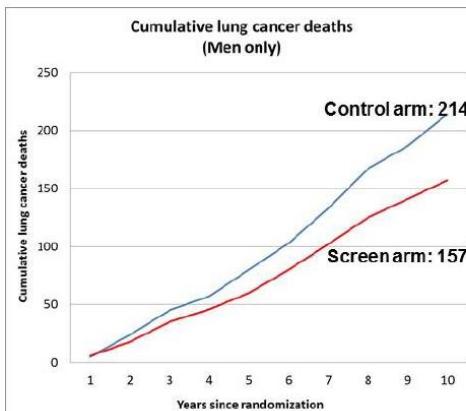
- OS

### Other endpoints

- DFS
- OS from recurrence or 2<sup>nd</sup> primary
- HRQoL
- Cost-effectiveness
- Prognostic signature

De Koning et al, WCLC 2018

## Early stage NSCLC > LDCT screening RCT [NELSON]



Lung cancer mortality rate ratio (95% CI)	Year 8	Year 9	Year 10
MALES	<b>0.75</b> P=0.015 (0.59-0.95)	<b>0.76</b> P=0.012 (0.60-0.95)	<b>0.74</b> P=0.003 (0.60-0.91)
FEMALES	<b>0.39</b> P=0.0037 (0.18-0.78)	<b>0.47</b> P=0.0069 (0.25-0.84)	<b>0.61</b> P=0.0543 (0.35-1.04)

De Koning et al, WCLC 2018

# האם מבחן סקירה

## כיאכט ?

- יותר ויותר גורמים בעולם ממליצים על סריקה.
- משרד הבריאות הקים ועדת רב-מקצועית לבחינת היישום בארץ.
- שאלות ובעיות עיקריות:
  - האם אוכלוסיות עם פרופיל סיכון שונה ירוויחו גם כן?
  - מהי תדירות הבדיקה הנדרשת (מידי שנה?)  
ולמשך כמה שנים (כל החיים?) ?



# האם מבחן סקירה?

- שאלות ובעיות עיקריות:
  - האם Cost-effective ?
  - בעיית "אבחון יתר" – גידולים שלא היו מגיעים בידי ביטוי קליני. פרוצדורות מיותרות ?
  - הגברת עישון ?
  - התפתחות גידולים משניים לקרינה ?



# האם מחלת סקירה?

- בשנת 2019 הוצע בסל הבריאות ולא התקבל
- הסיבות העיקריות לדחיה  
(נוסף לטיעונים שהועלו קודם):
  - חשש מסקירה "לא מקצועית" ע"י מכוניים מזרים
  - טענה כי מקור המימון (כולל תקני רפואיים נוספים הנדרשים לכך) צריכה לבוא ממוקורות אחרים.
- בשנת 2021 – הוחל "פילוט" במשרד הבריאות לסקירה מוקדמת של סרטן ריאות – פרויקט **תיג"ר** –  
לקראת התחלת פעילות



הַבָּאָתִים