PILOT™ Education Transforming PULMONARY CARE

Dyspnea and Disease Are Progressing

www.PILOTforPulmonary.org

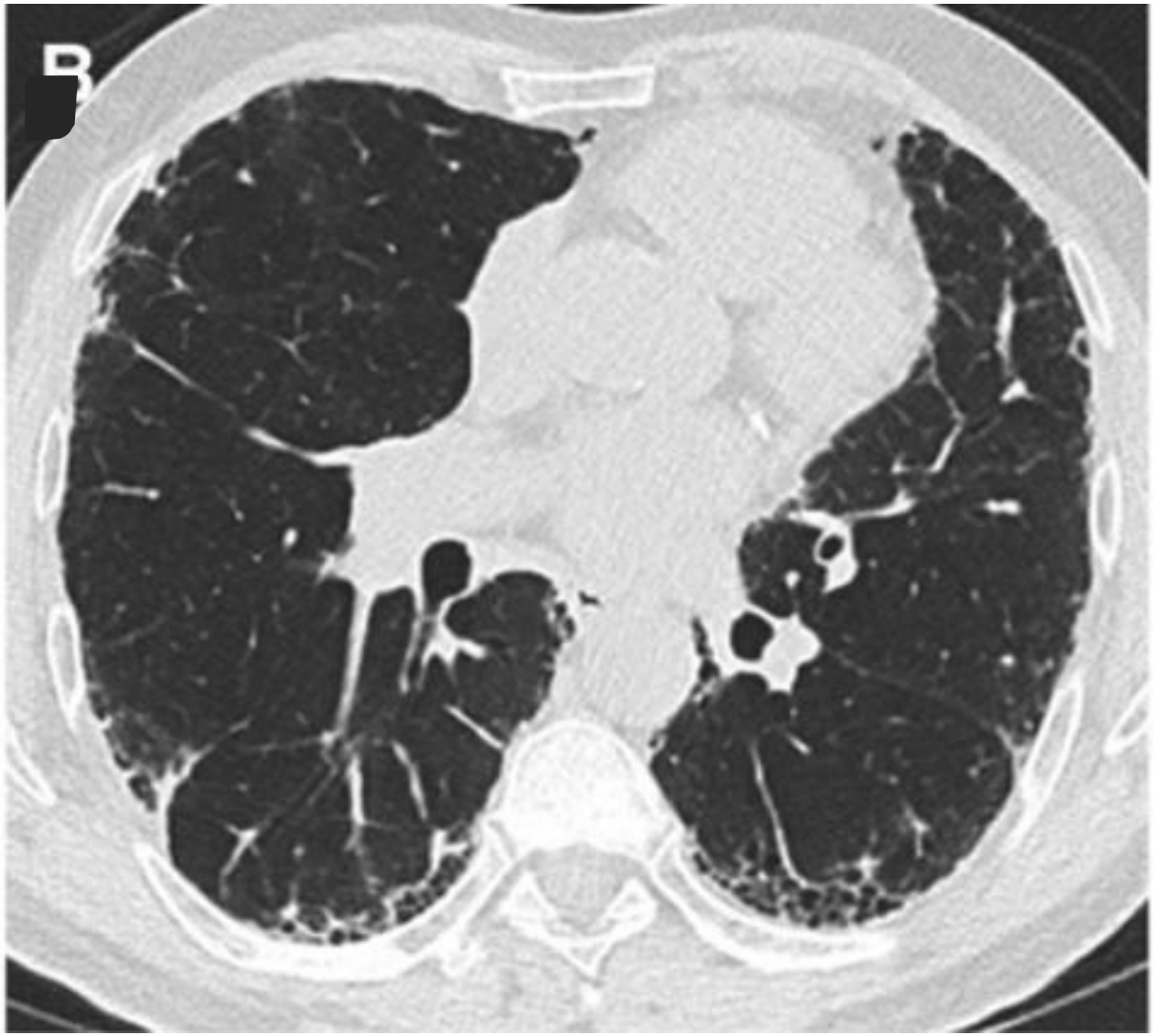
Workshop Description

- Facilitated interactive case discussion; faculty need to manage time so that all cases are reviewed/discussed
- Four different cases (IPF, PAH, asthma, COPD)
- Each case has a series of questions that will serve as a guide to the discussion.
- Slides are included within each section that may be useful to support discussion

Meet Jane: 63-year-old Female

- Lives in Kona, Hawaii
  - Provides educational talks about sea turtles for visitors at the beach in Kaloko-Honokohau National Park
- No PMH, former smoker
- No symptoms of SOB or cough
- Incidental ILD found on routine CXR

Jane's HRCT: UIP



Jane's Pulmonary Function Tests

- TLC = 3.61 (94% of predicted)
- FVC = 1.75 (76% of predicted)
- FEV1 = 1.45 (85% of predicted)
- FEV1/FVC = 83%
- DLCO = 14.31 (73% of predicted)
- DL/VA = 4.74 (100% of predicted)

Questions

- Is Jane a candidate for antifibrotic therapy?
  - If yes, which agent would you recommend for Jane?
- What should you include in your discussion regarding the risks and benefits of starting treatment?
- If she starts treatment, what can be expected if a dose adjustment is necessary to manage treatment-related side effects?

Jane: Six Months on Antifibrotic Therapy

- Six months after initiation of nintedanib, Jane presented to the clinic with complaint of increased DOE, now SOB after one block and one flight of stairs (was asymptomatic at baseline)

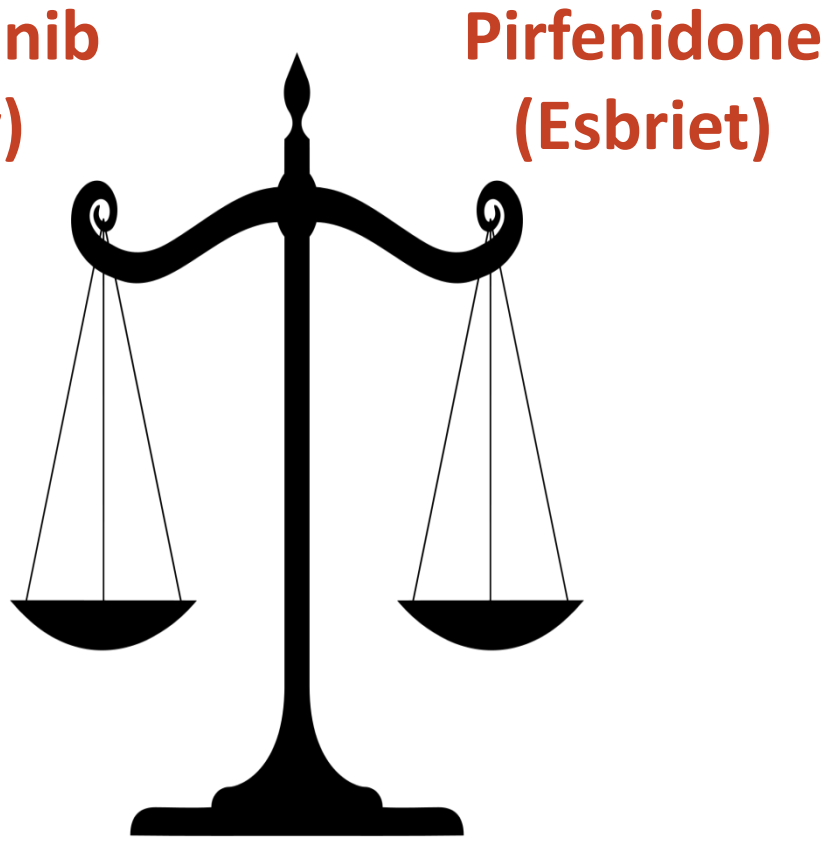
- PFTS obtained
  - Baseline: FVC 85%, FEV_1 90%, DLCO 67%
  - **Six months: FVC 72%, FEV_1 80%, DLCO 51%**

What Are Reasonable Management Options for Jane Now?

- ❑ Evaluate treatment adherence
- ❑ Stop nintedanib: It's not working
- ❑ Continue nintedanib: Disease progression does not = drug failure
- ❑ Add pirfenidone
- ❑ Switch to pirfenidone
- ❑ Refer for pulmonary rehabilitation
- ❑ Refer for lung transplant evaluation
- ❑ Hospice consultation

Factors Influencing Treatment Decisions

- Lifestyle
- Comorbidities
- Potential treatment-related side effects
- Patient preferences
- Realistic treatment expectations



Approved Antifibrotic Therapies for Patients with IPF

Pirfenidone

- FDA approval 2014
- Antifibrotic properties; exact mechanism of action unknown
- Orally administered, 801 mg, three times daily
- Nausea, **RASH/SUN SENSITIVITY**, dyspepsia/GERD

Nintedanib

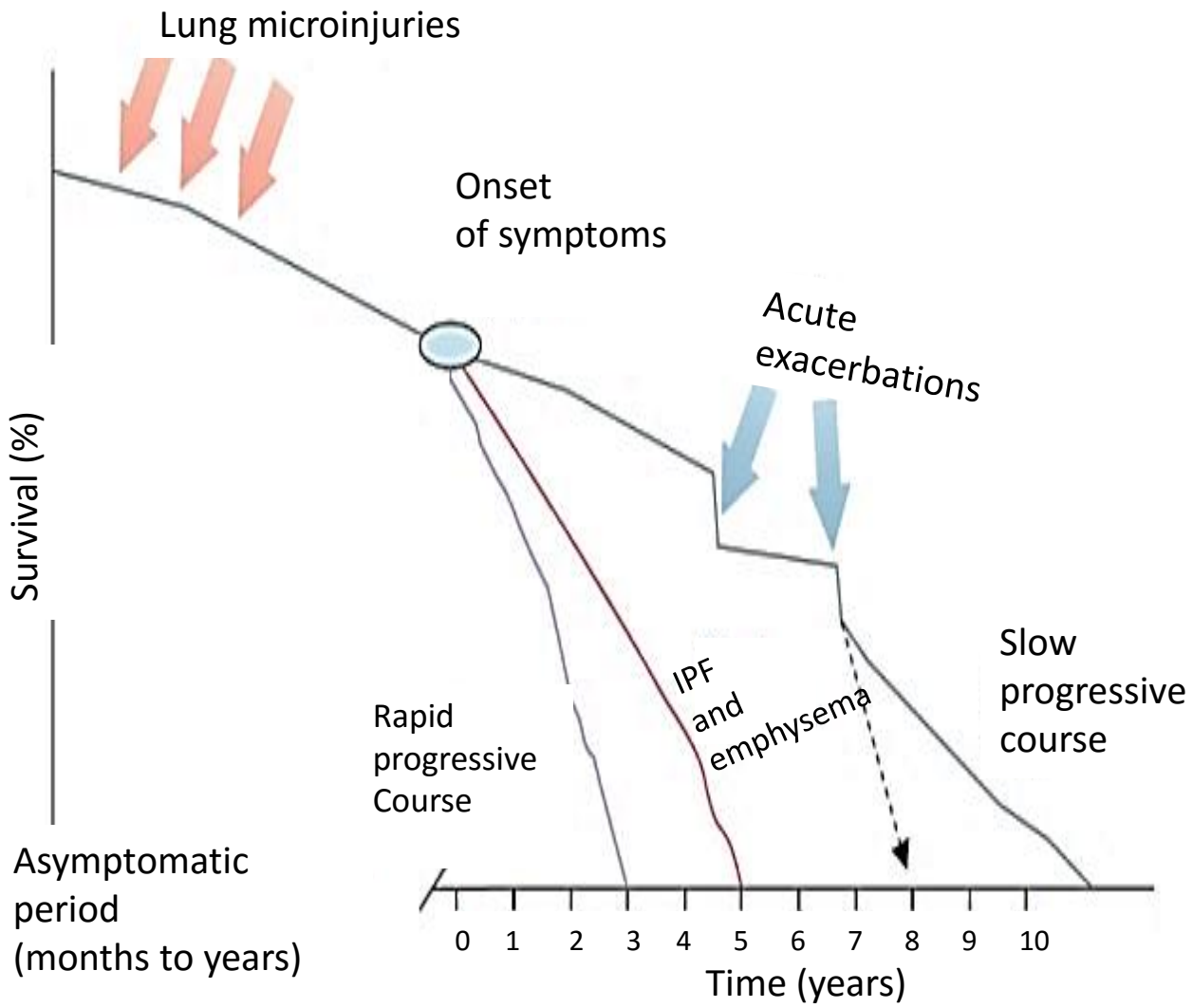
- FDA approval 2014
- Tyrosine kinase inhibitor; targets FGFR, PDGFR, VEGFR, FLT3
- Orally administered, 150 mg, two times daily
- Diarrhea, nausea

Pirfenidone. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022535s005lbl.pdf
Nintedanib. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/205832s004lbl.pdf
Galli JA, et al. *Respirology*. 2017;22:1171-1178.

Recommendations for Optimizing Treatment Adherence in Patients with IPF

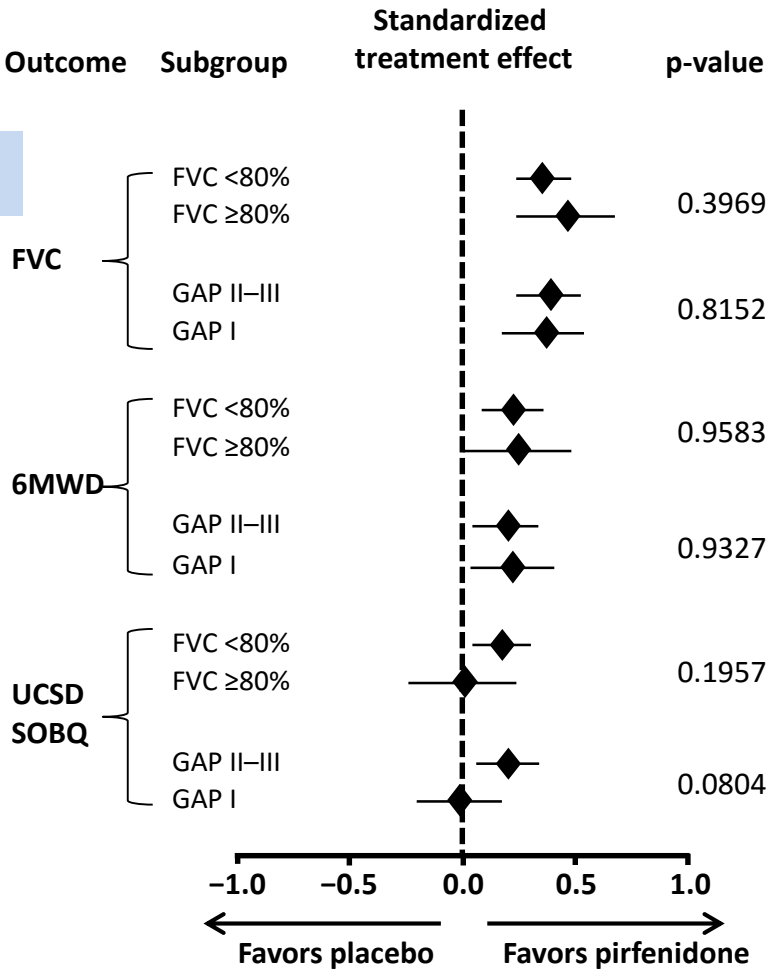
- Establish clear treatment expectations
  - Drugs are unlikely to improve symptoms
  - Partner with patient to manage any side effects
  - Unable to distinguish if drug “is working”
- Discuss the importance of treatment adherence
- Monitor and manage treatment-related side effects
- Implement dose reduction protocols, as appropriate
- Consider treatment switch for intolerable side effects despite dose adjustments and other symptom management strategies

The Course of IPF Is Variable



Does Disease Severity Matter?

Jane's baseline FVC = 85%



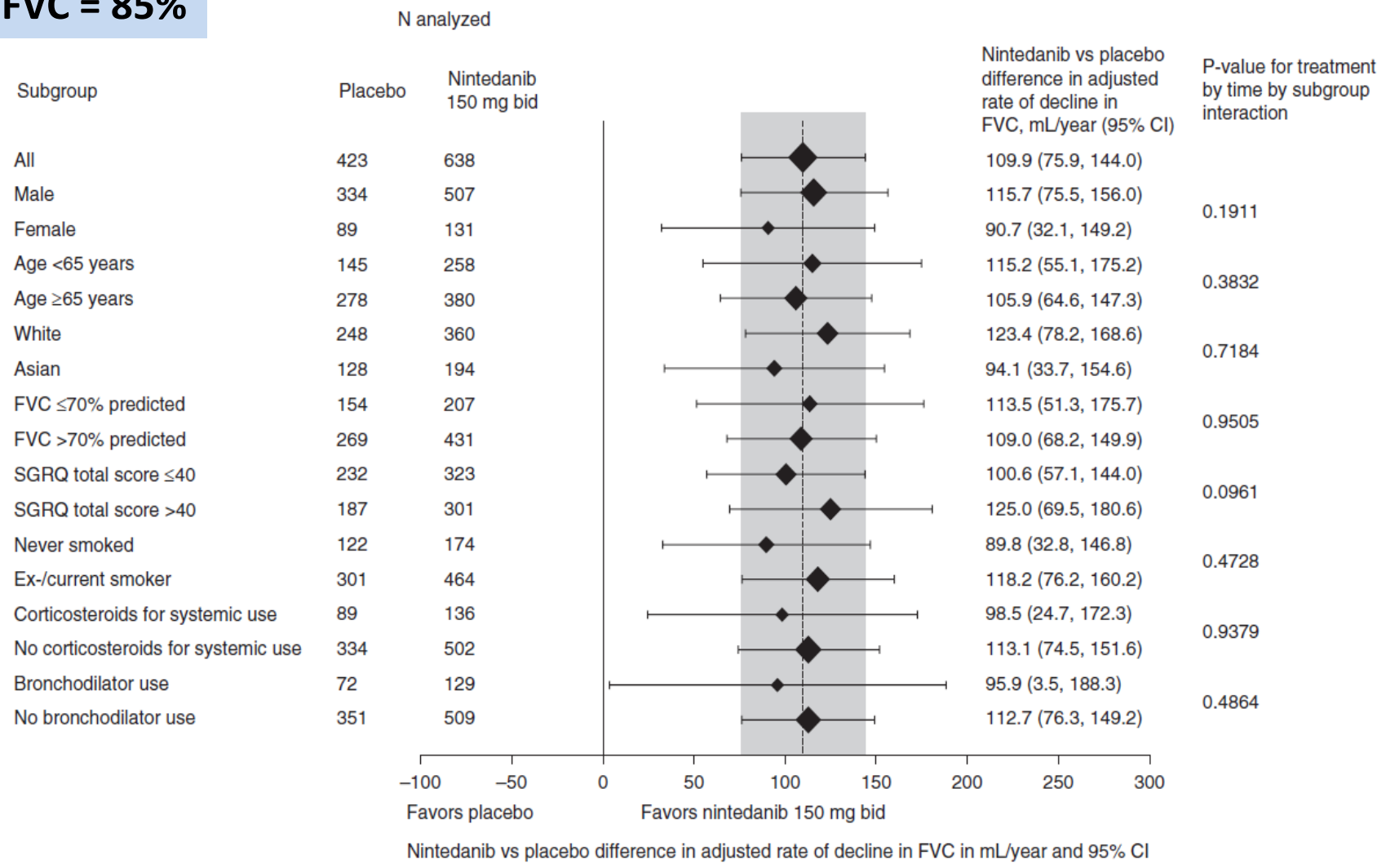
Pirfenidone was associated with decreases in the proportion of patients experiencing categorical declines in the three outcomes, with **no significant differences** between mild and moderate disease

6-MWD, 6-minute walk distance; UCSD SOBQ, University of California San Diego Shortness of Breath Questionnaire
RXUKESBR00231w/Date of preparation: May 2017

Albera C, et al. *Eur Respir J*. 2016;48:843–851.

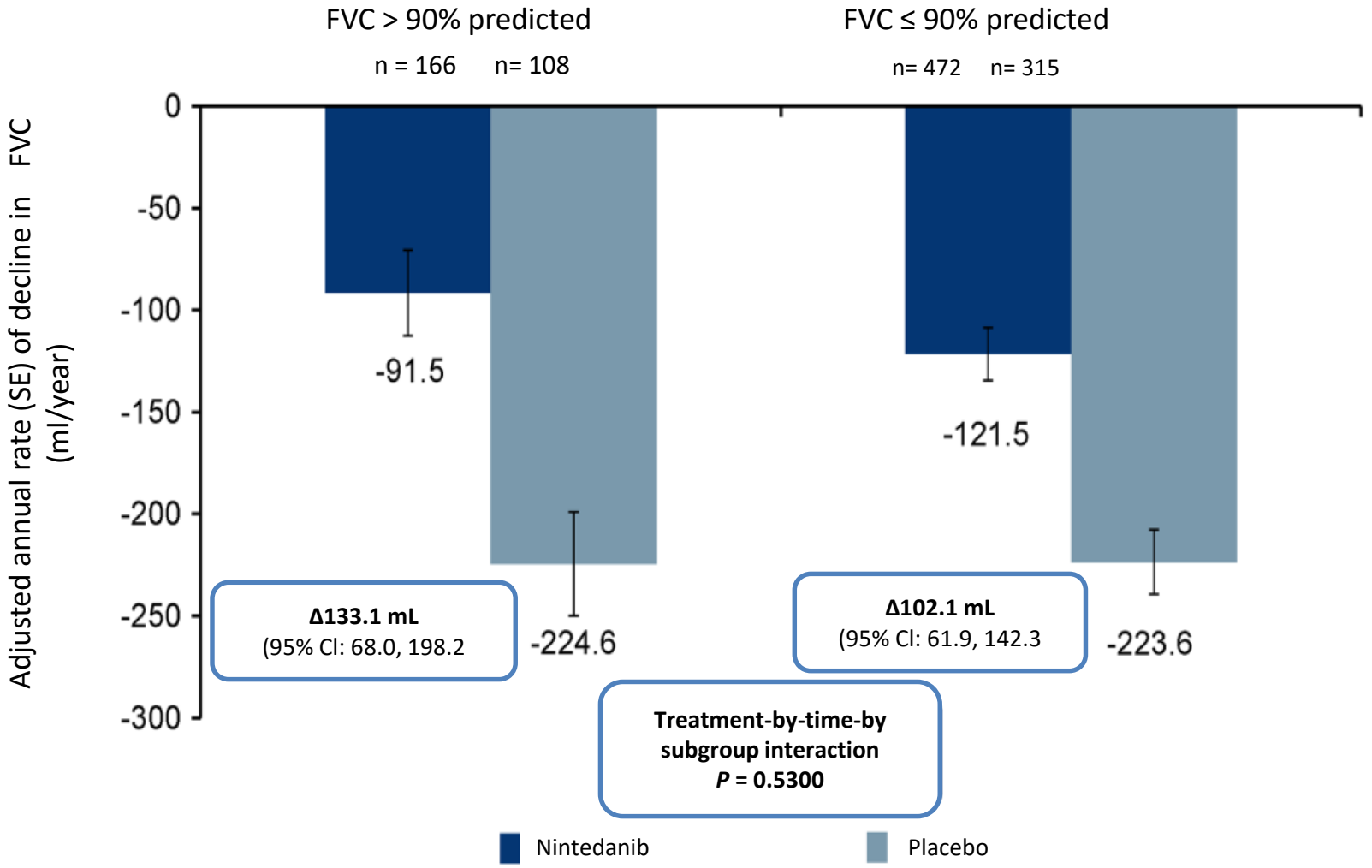
Consistent Effect of Nintedanib Across Patient Subgroups

Jane's baseline FVC = 85%



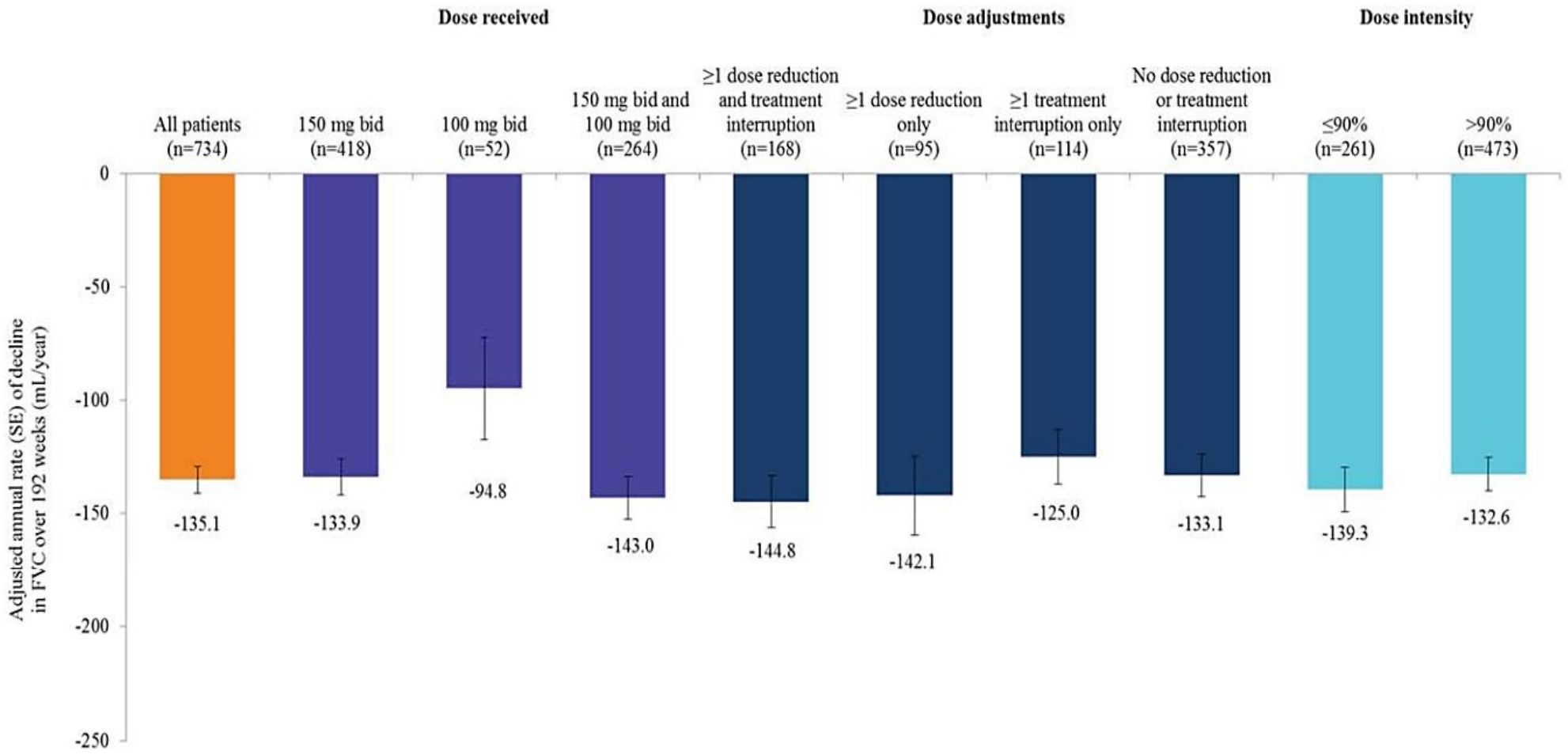
Costabel U, et al. *Am J Respir Crit Care Med*. 2016;193:178–185.

Nintedanib in Patients with Preserved Lung Function



Kolb M, et al. *Thorax*. 2017;72:340-346.

Annual Rate of Decline in FVC by Nintedanib Dose Adjustment/Intensity



Crestani B, et al. *Lancet Respir Med*. 2018 Sept 14. [Epub ahead of print]

Monitoring for Disease Progression

- Consider every three months:
  - PFTs (at least FVC and DLCO)
  - 6MWT (distance/nadir saturation)
  - O_2 requirement during activity
  - Comorbidities
  - Use of dyspnea and cough questionnaires
    - (UCSD, SGRQ, CQLQ, LCQ)
  - Assessment of overnight pulse oximetry to assess for nocturnal desaturation

- Repeat imaging:
  - Consider HRCT upon suspicion of clinical worsening
  - Consider CT angiogram if any suspicion for PE

At Each Visit

- Ask yourself and your patient:
  - Are we still comfortable with what we're doing?
  - Assess quality of life, challenges
  - Side effects of medications
  - Should we change anything?
  - Are there data to support doing anything differently?

- Determine whether your patient is progressing
  - If unsure, bring him/her back in six weeks and obtain another data point

Pirfenidone Effect in the Subsequent Six-Month Period After FVC Decline ≥ 10%

	Pirfenidone (N=34)	Placebo (N=68)	Δ	*P*-Value
≥ 10% decline in FVC or death	2 (5.9%)	19 (28%)	−79%	0.009
No further decline in FVC	20 (59%)	26 (38%)	+54%	0.059
Death	1 (2.9%)	14 (21%)	−86%	0.018

Nintedanib Effect After FVC Decline ≥ 10% in the First Six Months

Event in First Six Months	Outcome in Subsequent Six Months	Nintedanib (n = 46)	Placebo (n = 53)
Absolute percent predicted FVC decline of ≥10%	Further absolute FVC decline ≥10%	19.6%	18.9%
	Death	10.9%	13.2%

Event in First Six Months	Outcome in Subsequent Six Months	Nintedanib (n = 87)	Placebo (n = 89)
Relative % predicted FVC decline of ≥10%	Further relative FVC decline ≥10%	31.0%	24.7%
	Death	10.3%	14.6%

Richeldi L, et al. *Eur Respir J*. 2016;48:OA1814.
Richeldi L, et al. Presented as an oral presentation at ERS International Congress 2016.

Meet Sandra: 52-Year-Old Female

- Was diagnosed with PAH one year ago and has recently relocated
- She is in clinic today as a new patient
- Review of her medical records indicate that she was diagnosed as **WHO FC I**, she had a negative acute vasoreactivity test and no PH-treatment was initiated

Sandra: Risk Assessment

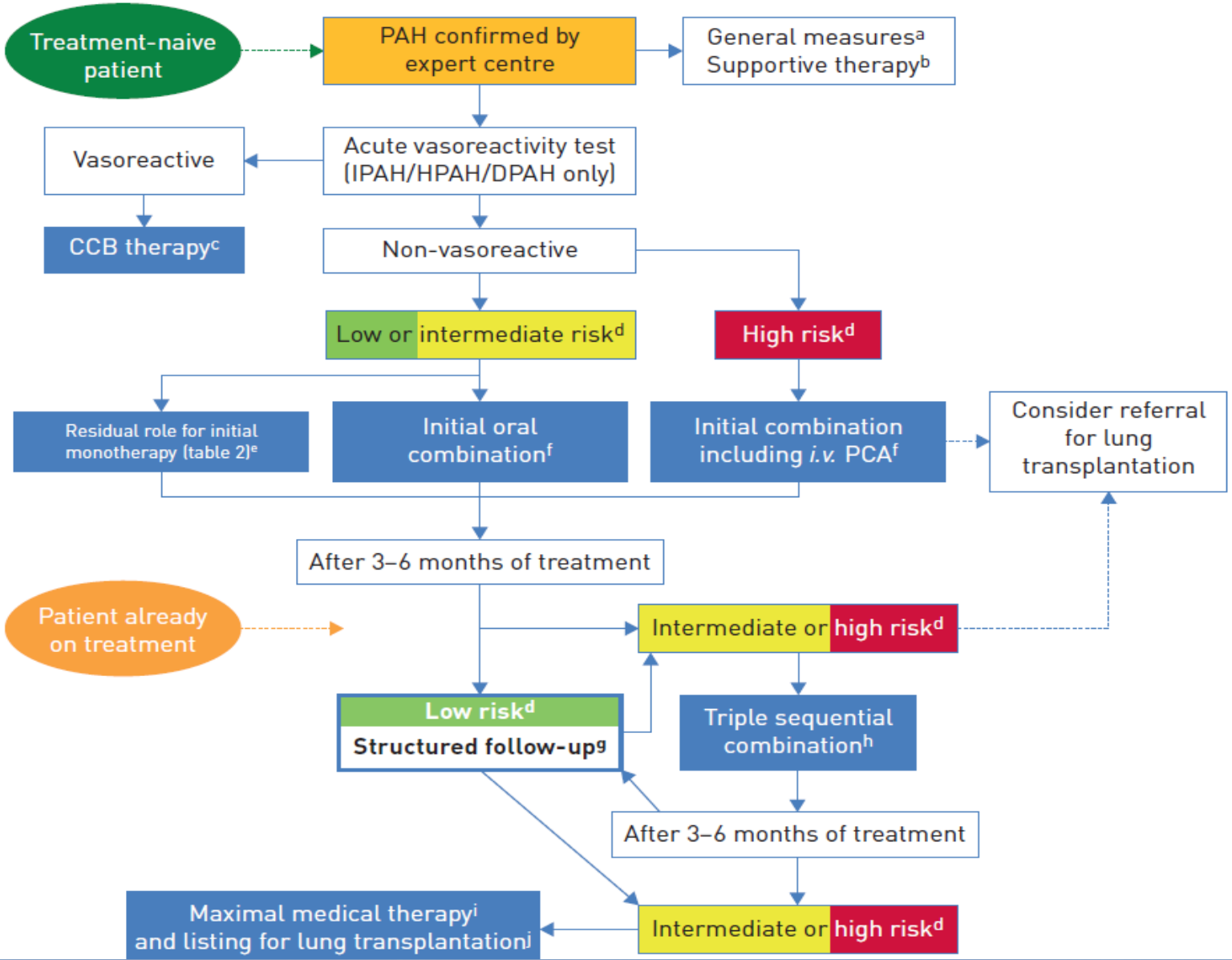
- Sandra is usually comfortable at rest, but since she has moved and is settling into her new home she is having difficulty with normal activities, not to mention the added effort associated with unpacking. She is frequently out of breath, quite fatigued and almost fainted a few times.

- No signs of right heart failure
- 6MWD 200 meters
- BNP: 250 ng/L; NT-proBNP: 600 ng/L
- Hemodynamics
  - RAP: 12 mm Hg
  - PA 69/30 (mPAP=43 mmHg)
  - Wedge pressure = 8 mmHg
  - CI: 2.2 l/min/m^2

Questions

- What is Sandra's WHO functional class?
- Has there been a change since her PAH diagnosis?
- What is your recommended treatment approach and why?
  - Pharmacotherapy?
  - Non-pharmacologic interventions, supportive care?
- How will you monitor Sandra?

6th World Symposium on Pulmonary Hypertension: Treatment Algorithm FOR PAH



Galiè N, et al. *Eur Respir J*. 2019;53:1801889.

Upon Confirmation of PAH

- Evaluate severity in a systematic and consistent manner.
- Coordinate care between local physicians and PH centers.
- Treat contributing causes of PH aggressively.
- Incorporate palliative care services in the management of PAH patients.
- Participate in supervised exercise activity as part of the integrated care of their disease.
- Maintain current immunization against influenza and pneumococcal pneumonia.
- Avoid pregnancy. When pregnancy does occur, we suggest care be provided at a pulmonary hypertension center.
- Avoid exposure to high altitude. When exposure to high altitude or air travel occurs, use supplemental oxygen as needed to maintain oxygen saturations > 91%.
- Avoid non-essential surgery. When surgery is necessary, we suggest care at a pulmonary hypertension center.

Evaluate Disease Severity to Inform Treatment Decisions

- Evaluate severity in a systematic and consistent manner
  - WHO FC
  - Exercise capacity
  - Echocardiographic, laboratory and hemodynamic variables

WHO Functional Class

Classification
Class I: Patients with PH but **without resulting limitation** of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.
Class II: Patients with PH resulting in **slight limitation** of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class III: Patients with PH resulting in **marked limitation** of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class IV: Patients with PH with **inability to carry out** any physical activity without symptoms. These patients manifest signs of right-sided heart failure. Dyspnea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity.

Currently Approved Medications for PAH

Class	Drug	Route of Administration	Dose
Prostacyclin derivatives	Epoprostenol*	IV infusion	2 ng/kg/min
			Increase as tolerated
	Iloprost	Inhaled	2.5 or 5.0 mg
			6-9 inhalations/d
	Treprostinil	Oral	0.25 mg bid or 0.125 mg tid
			Increase 0.125 mg bid every 3-4 d
		Inhaled	18-54 mg (3-9 inhalations)
			4 times daily
		Subcutaneous or IV infusion	1.25 ng/kg/min; increase 1.25 ng/kg/min per week based on clinical response
Endothelin receptor antagonists	Bosentan	Oral	125 mg twice daily
	Ambrisentan	Oral	5 or 10 mg once daily
	Macitentan	Oral	10 mg once daily
Phosphodiesterase type-5 inhibitors	Sildenafil	Oral	20 mg every 8 h
		IV injection	
	Tadalafil	Oral	40 mg once daily
Soluble guanylate cyclase stimulator	Riociguat	Oral	0.5-1.0 mg every 8 h (increase 0.5 mg every 2 wk as tolerated to maximum dose 2.5 mg)
Prostacyclin receptor agonists	Selexipag	Oral	200 mg twice daily
			Increase as tolerated to maximum dose of 1600 mg twice daily

Klinger JR, et al. *CHEST*. 2019 January 17. [Epub ahead of print]

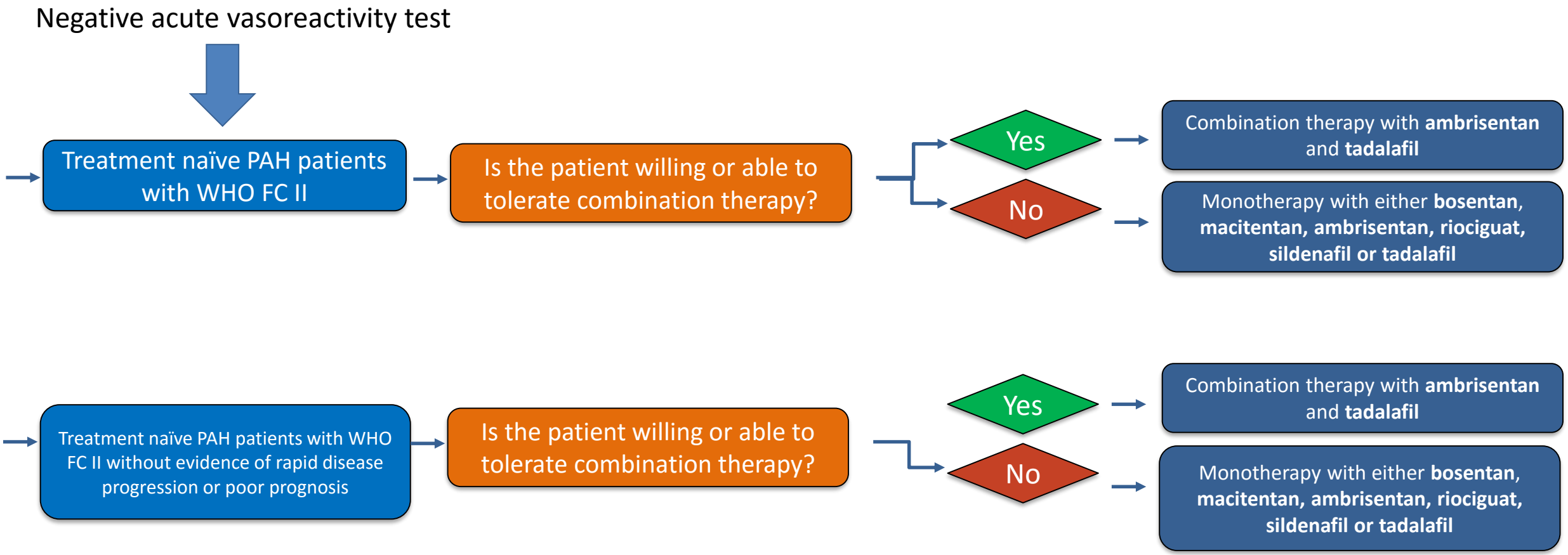
Treatment Goals

- Achieving low-risk status, which is:
  - Good exercise capacity
  - Good quality of life
  - Good RV function
  - Low mortality risk

Goal: WHO-FC II whenever possible, with normal/near-normal 6MWD

Treatment Naïve Patients: WHO FC II and III

Initial combination therapy with ambrisentan and tadalafil to improve 6MWD



Klinger JR, et al. *CHEST*. 2019 January 17. [Epub ahead of print]

Meet Charles: 48-year-old male

- History of wheezing after colds as a child
- At age 40, caught a “bad cold” and developed a respiratory infection lasting several weeks
- Since then, has had infections associated with wheezing four-six times per year
- At age 44, began to have chronic postnasal drip, persistent coughing and wheezing despite treatment
  - Mometasone/formoterol MDI 200 mcg/5 mcg, two puffs BID
  - Montelukast 10 mg QHS
  - Tiotropium 1.25 mcg, two puffs QD
  - Fluticasone propionate nasal spray, one spray per nostril BID
- Currently uses his rescue albuterol inhaler three-four times/day
- Awakens with nonproductive cough and wheezing ~three nights/wk
- Two 10-d courses of prednisone in the past six months for severe dyspnea, cough, wheezing, chest tightness

Charles (con't)

- Review of systems: can't smell or taste his food
- Past medical history: hypertension, hyperlipidemia, gout
- Drug allergies: severe dyspnea and chest tightness after taking an effervescent antacid/pain relief medication
- Medications: above medications + amlodipine, simvastatin, allopurinol
- Environmental history: He lives in a newer home in the Los Angeles area with three pet dogs
- Family history: father with seasonal hay fever
- Social history: He smoked one pack of cigarettes per day from age 16 to 38 years

Charles: Physical Exam

- Thin, looks older than his stated age, in no acute distress
- HEENT: bilateral inferior turbinate swelling with right-sided blue-grey, grape-like mass
- Lungs: bilateral mild expiratory wheezing, diffuse with occasional rhonchi
- Heart: normal heart sounds, no murmur
- Extremities: trace pedal edema, no cyanosis or clubbing

Charles: Lung Function and Lab Tests

Parameter	Pre-bronchodilator Absolute (L) & %predicted	Post-bronchodilator Absolute (L) & %predicted	Post-bronchodilator % change
FVC	3.08 (72%)	3.14 (73%)	+2%
FEV_1	1.88 (53%)	2.11 (59%)	+12%
FEV_1/FVC	0.61	0.67	NA
$FEF_{25-75\%}$	28%	35%	+25%

- CBC: normal WBC, hemoglobin; eosinophils (from differential) = 778/mcl
- Specific IgE assay: positive to elm tree and ragweed pollen, *Aspergillus fumigatus* (mold)
- Total IgE = 183 IU/ml

Charles: Questions

1. What is your preliminary diagnosis?
2. Highlight key aspects of his history and physical that can help inform your treatment decisions and recommendations.
3. What additional history would be helpful?
4. What is the significance of his “bad cold” at age 40?
5. What additional testing would you do?
6. What is Charles’ asthma phenotype?
7. What therapeutic changes would you make?
   - What would be your initial plan and for how long?
   - What would be your follow-up plan? [develop an asthma action plan]

Name: Charles Today's Date: Clinic Visit

ASTHMA CONTROL TEST™

Know your score.

The Asthma Control Test™ provides a numerical score to help you and your healthcare provider determine if your asthma symptoms are well controlled.

Take this test if you are 12 years or older. Share the score with your healthcare provider.

Step 1: Write the number of each answer in the score box provided.

Step 2: Add up each score box for the total.

Step 3: Take the completed test to your healthcare provider to talk about your score.

IF YOUR SCORE IS 19 OR LESS, **Your asthma symptoms may not be as well controlled as they could be. No matter what the score, bring this test to your healthcare provider to talk about the results.**

NOTE: If your score is 15 or less, your asthma may be very poorly controlled. Please contact your healthcare provider right away. There may be more you and your healthcare provider could do to help control your asthma symptoms.

					SCORE
1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?					
All of the time **[1]**	Most of the time **[2]**	Some of the time **[3]**	A little of the time **[4]**	None of the time **[5]**	3
2. During the past 4 weeks, how often have you had shortness of breath?					
More than Once a day **[1]**	Once a day **[2]**	3 to 6 times a week **[3]**	Once or twice a week **[4]**	Not at all **[5]**	3
3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?					
4 or more nights a week **[1]**	2 to 3 nights a week **[2]**	Once a week **[3]**	Once or twice **[4]**	Not at all **[5]**	2
4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?					
3 or more times per day **[1]**	1 to 2 times per day **[2]**	2 or 3 times per week **[3]**	Once a week or less **[4]**	Not at all **[5]**	1
5. How would you rate your asthma control during the past 4 weeks?					
Not Controlled at All **[1]**	Poorly Controlled **[2]**	Somewhat Controlled **[3]**	Well Controlled **[4]**	Completely Controlled **[5]**	2

TOTAL: 11

Asthma Action Plan

AMERICAN LUNG ASSOCIATION.

Name _____ **DOB** ____/____/_____

Severity Classification ☐Intermittent ☐Mild Persistent ☐Moderate Persistent ☐Severe Persistent

Asthma Triggers (list) _____

Peak Flow Meter Personal Best _____

Green Zone: Doing Well

Symptoms: Breathing is good – No cough or wheeze – Can work and play – Sleeps well at night
Peak Flow Meter _____ (more than 80% of personal best)

Control Medicine(s)	Medicine	How much to take	When and how often to take it
	_____	_____	_____
	_____	_____	_____

Physical Activity ☐Use albuterol/levalbuterol ____ puffs, 15 minutes before activity
☐with all activity ☐when you feel you need it

Yellow Zone: Caution

Symptoms: Some problems breathing – Cough, wheeze, or chest tight – Problems working or playing – Wake at night
Peak Flow Meter _____ to _____ (between 50% and 79% of personal best)

Quick-relief Medicine(s) ☐Albuterol/levalbuterol ____ puffs, every 4 hours as needed

Control Medicine(s) ☐Continue Green Zone medicines
☐Add _____ ☐Change to _____

You should feel better within 20–60 minutes of the quick-relief treatment. If you are getting worse or are in the Yellow Zone for more than 24 hours, THEN follow the instructions in the RED ZONE and call the doctor right away!

Red Zone: Get Help Now!

Symptoms: Lots of problems breathing – Cannot work or play – Getting worse instead of better – Medicine is not helping
Peak Flow Meter _____ (less than 50% of personal best)

Take Quick-relief Medicine NOW! ☐Albuterol/levalbuterol ____ puffs, _____ (how frequently)

Call 911 immediately if the following danger signs are present
- Trouble walking/talking due to shortness of breath
- Lips or fingernails are blue
- Still in the red zone after 15 minutes

Emergency Contact Name _____ Phone (_____) _____-_____

Healthcare Provider Name _____ Phone (_____) _____-_____

1-800-LUNGUSA | LUNG.org

Date ____/____/_____

ERS/ATS: Uncontrolled Asthma

At least one of the following:

1) Poor symptom control: ACQ consistently > 1.5, ACT < 20 (or "not well controlled" by NAEPP/GINA guidelines)
2) Frequent severe exacerbations: ≥ 2 bursts of systemic CS (> 3 days each) in the previous year
3) Serious exacerbations: at least one hospitalization, ICU stay or mechanical ventilation in the previous year
4) Airflow limitation: after appropriate bronchodilator withhold FEV_1< 80% predicted (in the face of reduced FEV_1/FVC defined as less than the lower limit of normal)

Many patients with severe asthma are not well-controlled with standard therapy

Abbreviations: ACQ: Asthma Control Questionnaire; ACT: Asthma Control Test; NAEPP: National Asthma Education and Prevention Program.

Asthma Phenotypes and Endotypes

- **Phenotype:** clinical characteristics based upon genetic makeup and environmental exposures

- **Endotype:** specific phenotype with well-characterized pathophysiologic (molecular) mechanism
  - **T2 cytokines (IL-4, IL-5, IL-13):** dominant cytokines in airways of 60 – 70% of patients with asthma
  - **Cell sources of IL-5 and IL-13:** TH2 cells, type 2 innate lymphoid cells (ILC-2), mast cells
  - T2 gene expression correlates with worsening asthma control

Corren J. *Discov Med*. 2013;15:243-249.
Klein Wolterink RG, et al. *Eur J Immunol.* 2012;42:1106-1116.

Type 2 vs Non-Type 2 Asthma: Basic Distinctions

Type 2 Asthma

- More severe
- High expression of Th2-cell cytokines in the airways
- Airway and systemic eosinophilia
- Responsive to corticosteroids
- Responsive to inhibitors of type 2 inflammation

Non-Type 2 Asthma

- Less severe
- Low expression of Th2-cell cytokines in the airways
- Absence of airway and systemic eosinophilia
- Lack of responsiveness to corticosteroids
- Lack of responsiveness to inhibitors of type 2 inflammation

Fahy J. *Nat Rev Immunol.* 2015;15:57-65.

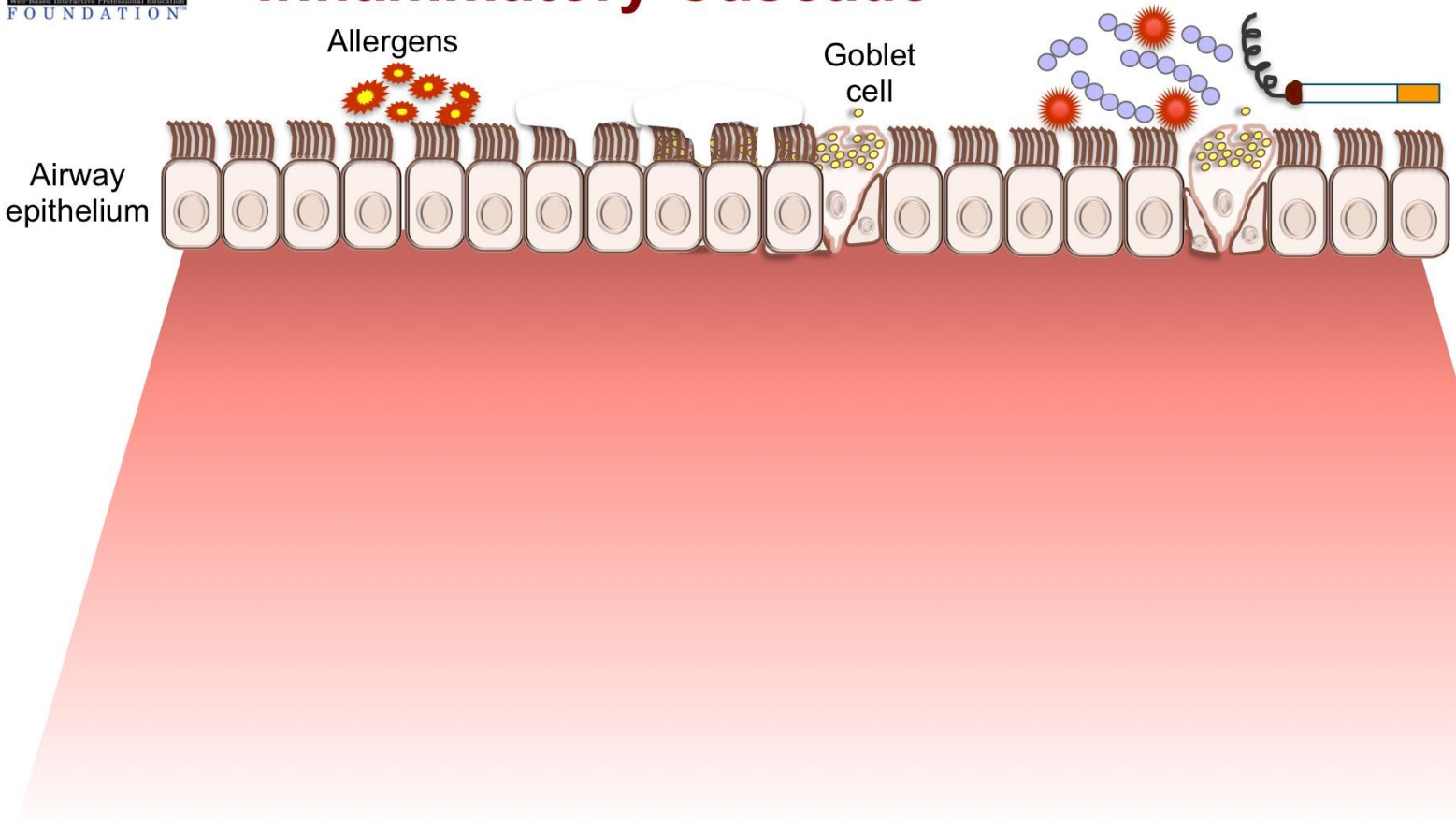
Severe Asthma Phenotypes and Endotypes

Endotype	Phenotype	Clinical/Physiologic Characteristics
Type 2 with variable eosinophilia	Early-onset, allergic	• History of atopic dermatitis and allergic rhinitis • May have chronic rhinosinusitis
Type 2 with marked eosinophilia; leukotrienes important in AERD	Late-onset, less allergic	• Often develops after chronic rhinosinusitis/nasal polyps; may be associated with AERD • Severe airway obstruction
Non-Type 2 with minimal or no eosinophilia	Late-onset, obesity-related, nonallergic	• Relatively normal bronchial responsiveness; minimal or no allergic comorbidities
	Late-onset, nonallergic	• Poorly characterized • May have significant LRT infection or GERD

Abbreviations: AERD = aspirin-exacerbated respiratory disease; LRT = lower respiratory infection; GERD = gastroesophageal reflux disease.

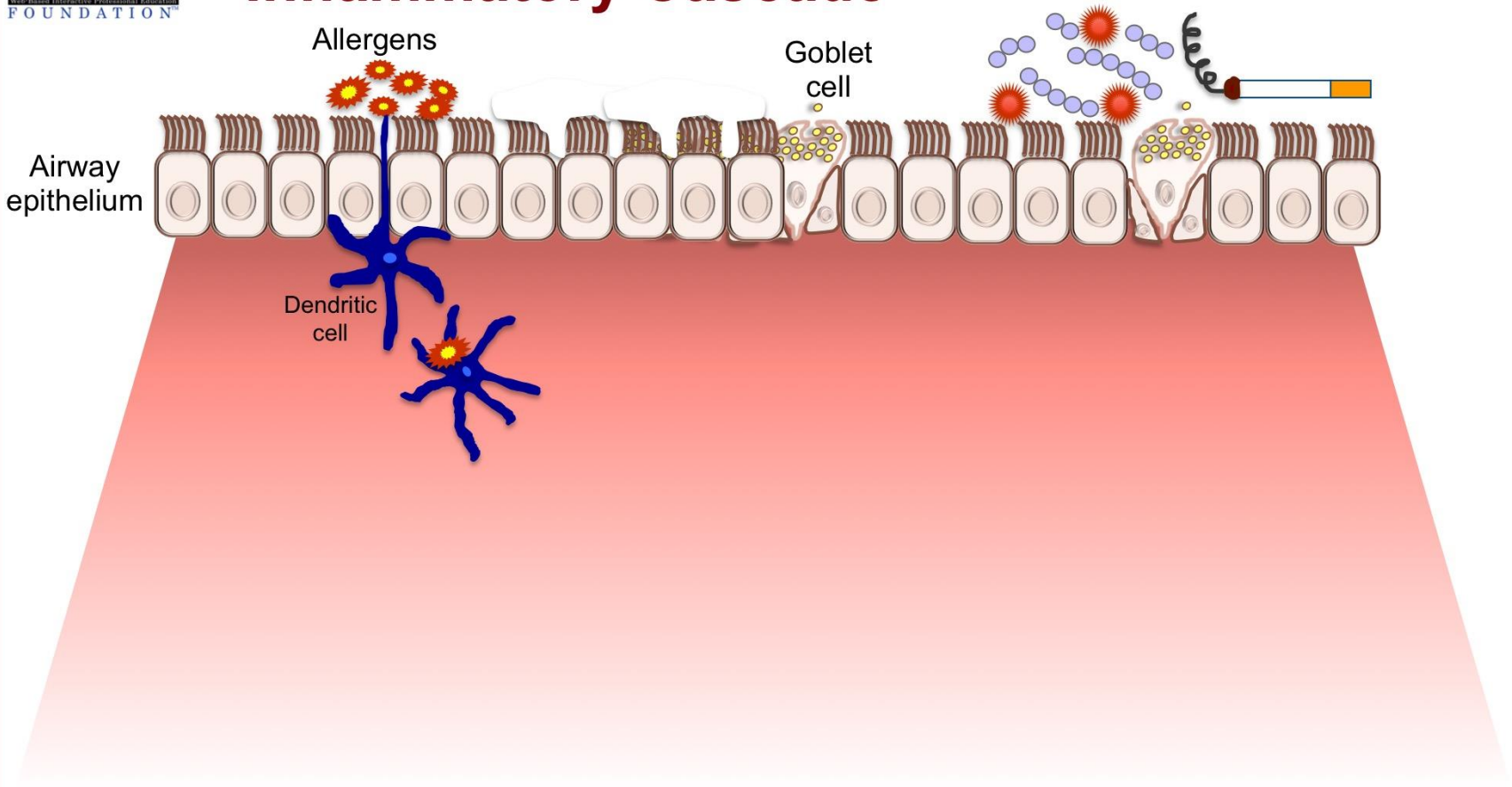
Wenzel SE. *Nat Med.* 2012;18:716-725.
Trejo Bittar HE, et al. *Ann Rev Pathol Mech Dis*. 2015;10:511-545.
Corren J. *Discov Med*. 2013;15:243-249.

Inflammatory Cascade



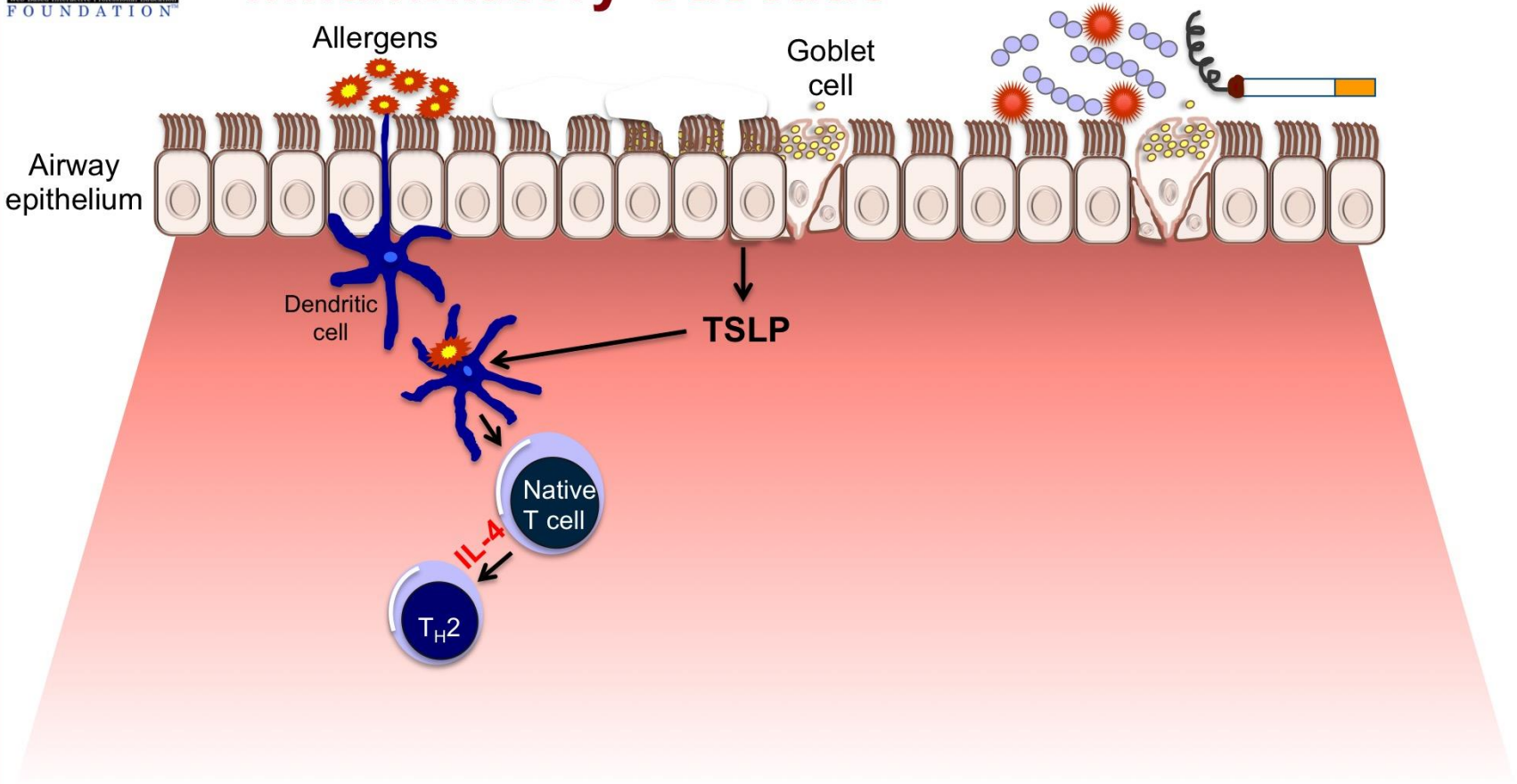
Allergic Eosinophilic Airway Inflammation

Inflammatory Cascade



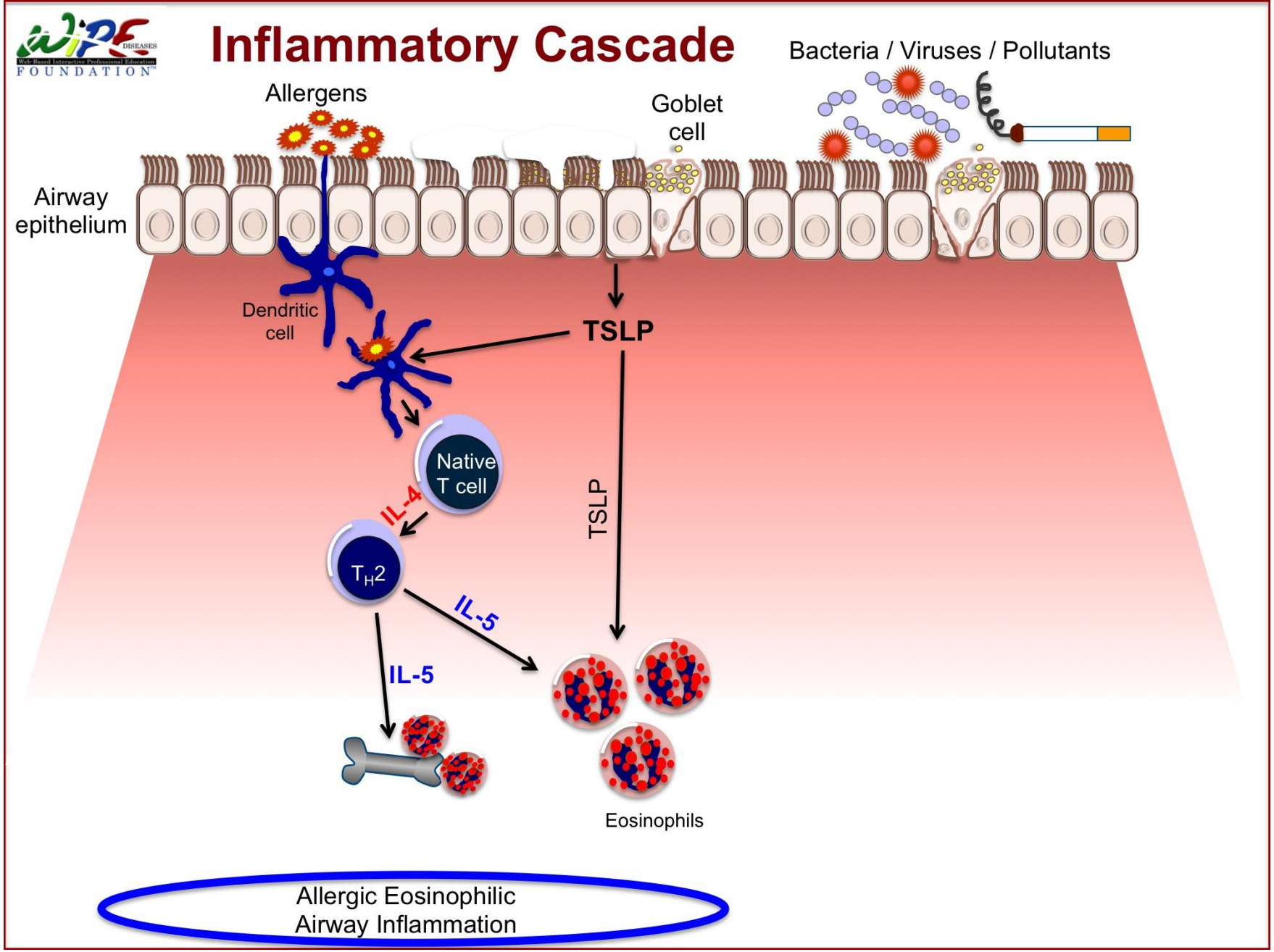
Allergic Eosinophilic Airway Inflammation

Inflammatory Cascade

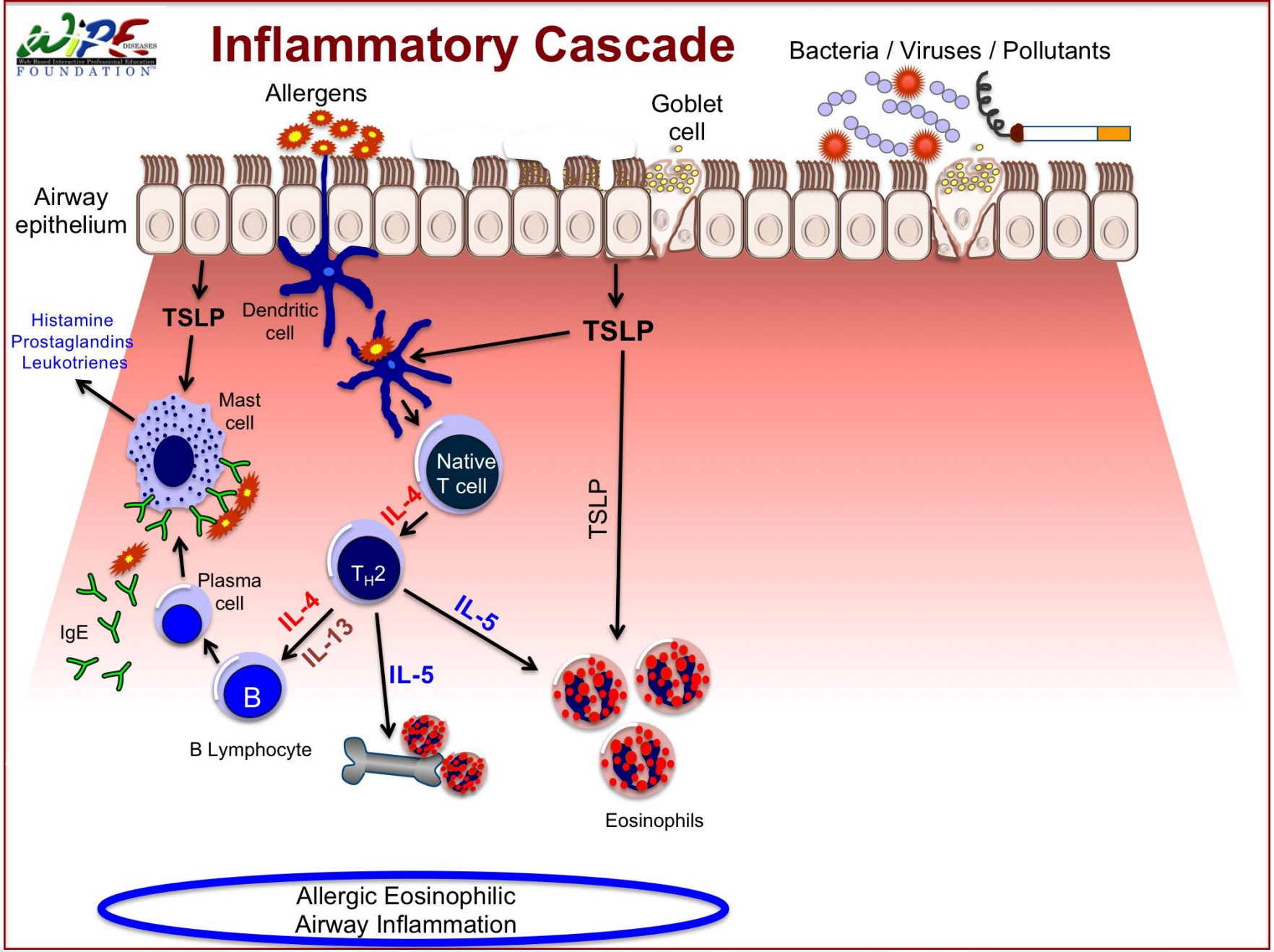


Allergic Eosinophilic Airway Inflammation

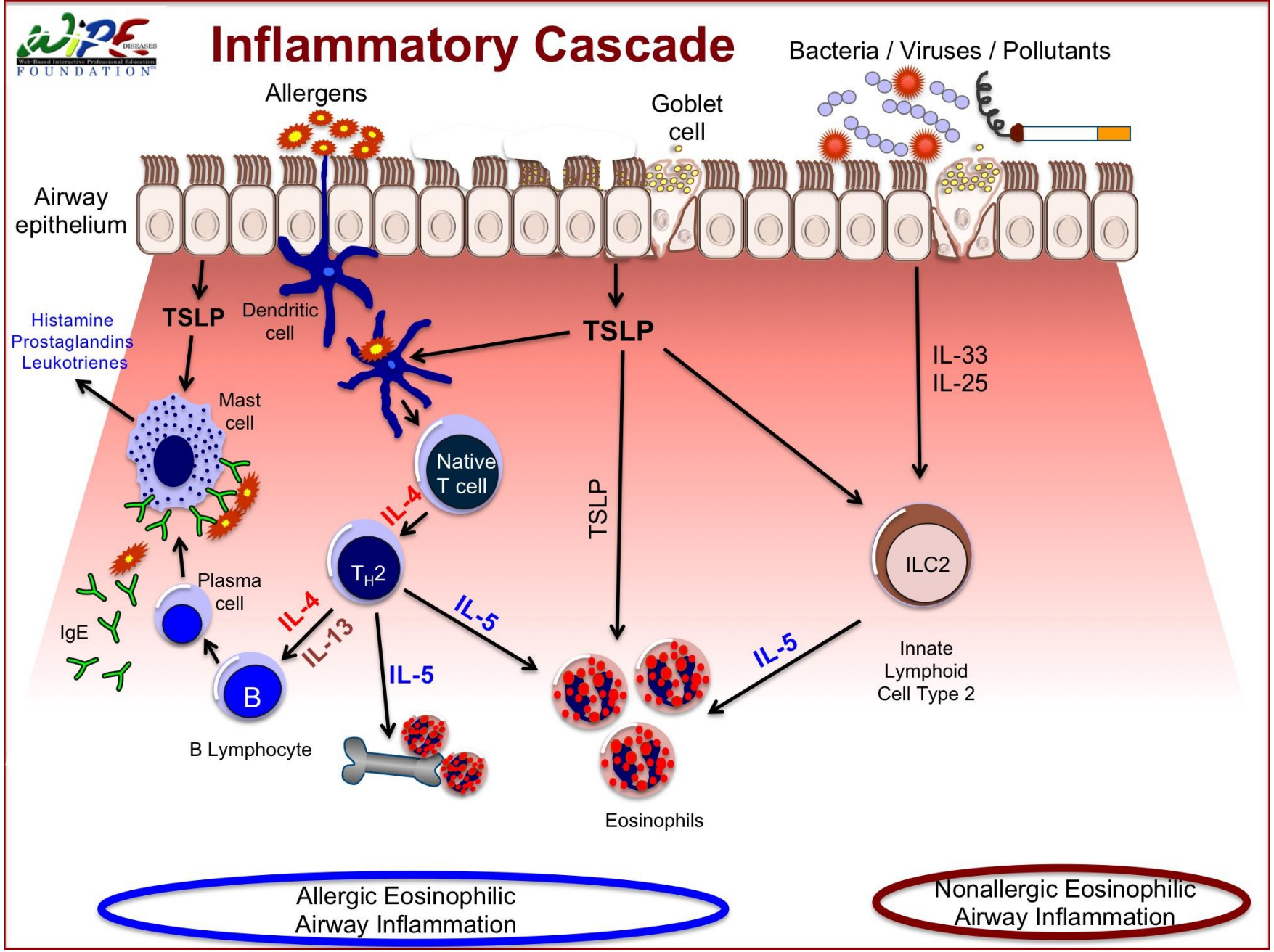
Inflammatory Cascade



Inflammatory Cascade



Inflammatory Cascade



Goals of Asthma Management

- *Achieve disease control*
  - Reduce frequency and severity of symptoms
  - Reduce rescue inhaler use
  - Increase physical activity
  - Improve in lung function
- *Reduce future risk of*
  - Exacerbations
  - Airway damage
  - Adverse effects of asthma medications

GINA. Global Strategy for Asthma Management and Prevention. Available from: http://ginasthma.org/gina-reports/.
Batemen ED, et al. *J Allergy Clin Immunol.* 2010;125:600-608.

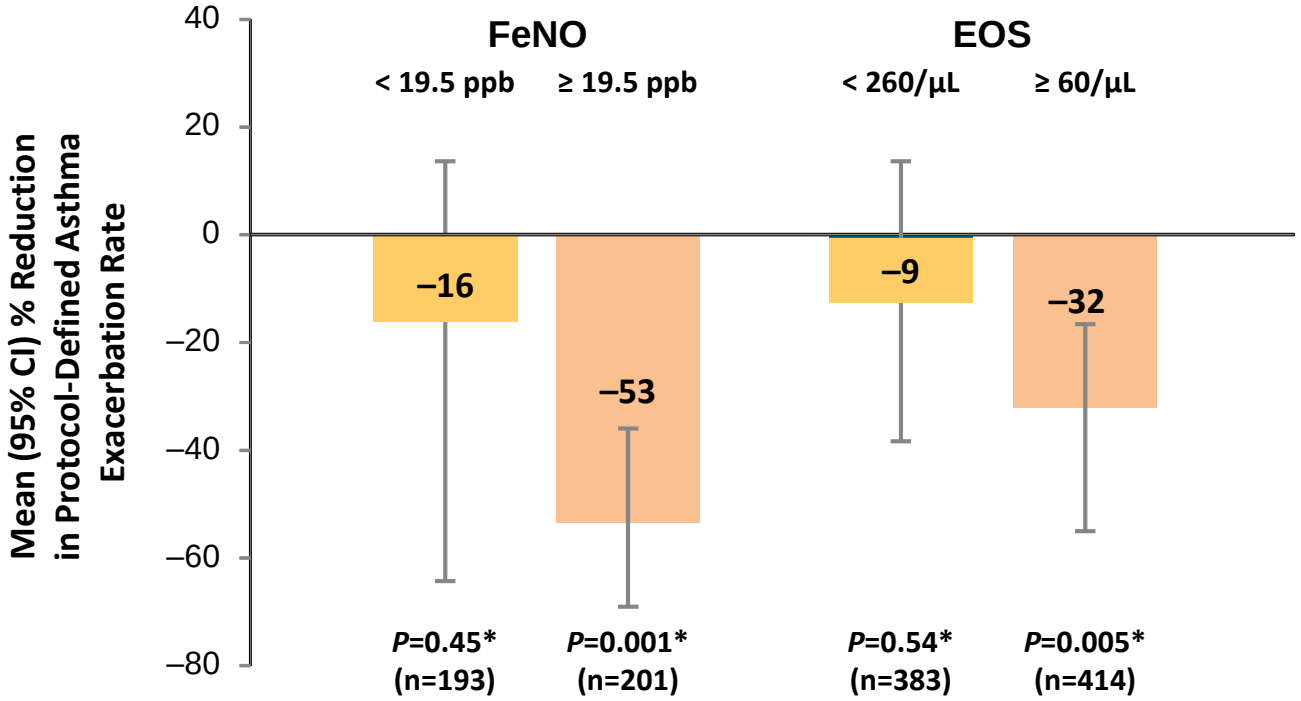
Monoclonal Antibody Treatments Approved or in Late Development and Their Targets

Treatment	Target
Omalizumab* (Xolair)	IgE
Mepolizumab* (Nucala)	IL-5
Reslizumab* (Cinqair)	IL-5
Benralizumab* (Fasenra)	IL-5Rα
Dupilumab* (Dupixent)	IL-4Rα (IL-4, IL-13)
Tezepelumab‡ (Currently no brand name)	TSLP

*FDA-approved for asthma.

‡Phase 2 clinical trial for treatment of severe asthma is complete; a phase 3 trial is recruiting.

Biomarkers May Predict Reductions in Exacerbations



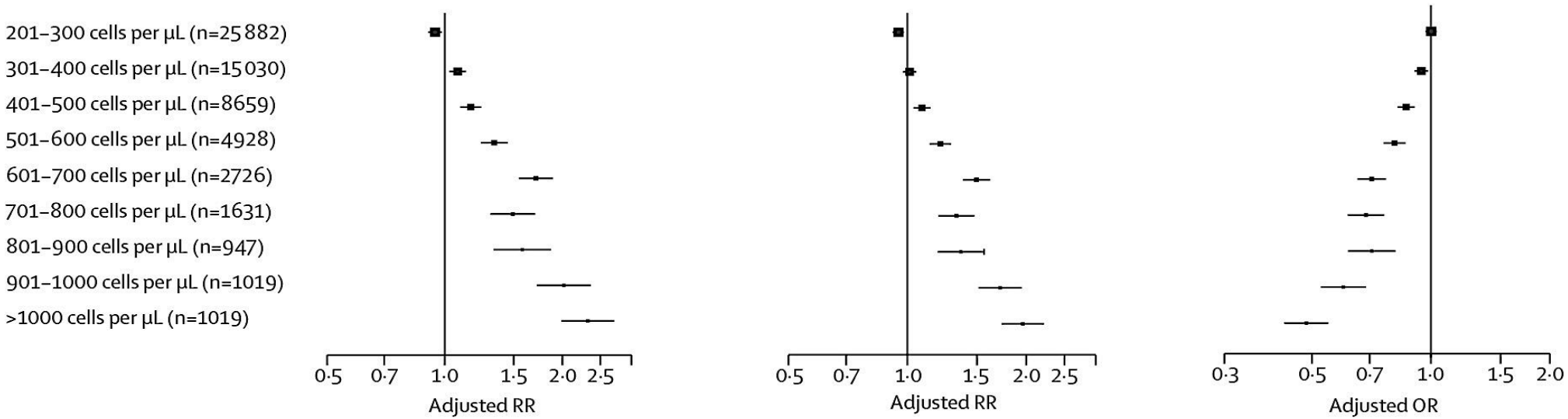
*Exacerbation reduction *P* values, omalizimab vs. placebo in each biomarker subgroup

Greater prevention of exacerbations with omalizumab was seen in patients with high individual T2 biomarkers (EOS, FeNO)†

†Greater prevention of exacerbations was also seen in patients with high periostin (≥50 ng/mL), though the difference compared to patients with low periostin (<50 ng/mL) was not significant (*P* = 0.07).

Blood Eosinophil Counts and Risk of Asthma Exacerbations

Claims database analysis examining eosinophil count and exacerbations requiring systemic CS or ER/hospital care



Severe Exacerbations

Acute Respiratory Events

Overall Asthma Control

Meet Jeff: 65-year-old male

- Diagnosed with COPD when he was 55
- Smoker: 22 pack/year; trying to quit, currently smoking five cigarettes per day
- Dyspnea on moderate exertion and occasional cough and sputum, occasional awakenings at night

Jeff: History

- Past history:
  - Childhood asthma, troublesome until age 12
  - Myocardial infarction four years ago
  - Diabetes mellitus and hypercholesterolemia
  - ‘Walking pneumonia’ five years ago treated with antibiotics
- Exacerbations
  - Twice last year, received short courses of antibiotics and oral steroids
- mMRC Dyspnea Score = 2

Jeff: Current Medications

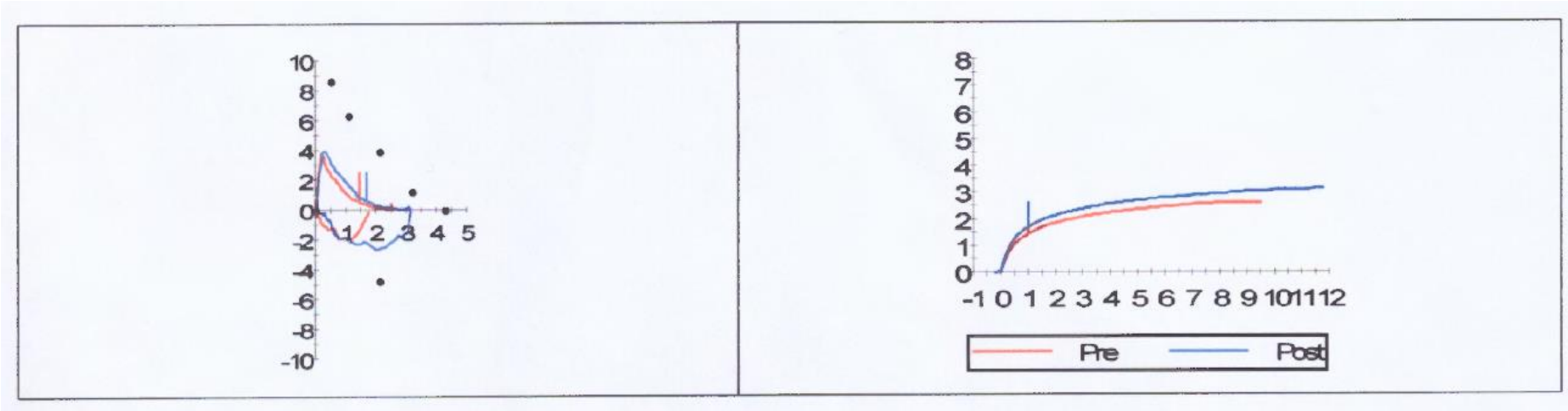
- Metformin 500 mg twice daily
- Atorvastatin 20 mg once daily
- ASA 81 mg once daily
- Currently taking tiotropium once daily and is on short acting beta$_2$-agonist, when needed

Jeff: Exam and Evaluation

- Physical findings:
  - Diminished air entry on lung auscultation, otherwise normal
- Labs
  - Hemoglobin: 11 g/dL
  - MCV: 89 fL
  - WBC: 10 x 10^3/µL
  - Eosinophils: 300/µL
  - Neutrophils: 55%
- CXR: hyperinflation, otherwise normal

Jeff: Pulmonary Function Test

		Pred	LLN	ULN	Pre Actual	% Pred	Post Actual	% Pred	% Chng
-- Spirometry --									
FVC (L)		4.25	3.41	5.09	2.61	61	3.15	74	+20
FEV1 (L)		3.29	2.58	4.00	1.46	44	1.70	51	+17
FEV1/FVC (%)		77	68	86	56	72	54	70	-3



2019 GOLD ABCD Assessment Tool

Spirometrically confirmed diagnosis → **Assessment of airflow limitation** → **Assessment of symptoms/risk of exacerbations**

Post-bronchodilator $FEV_1/FVC < 0.7$

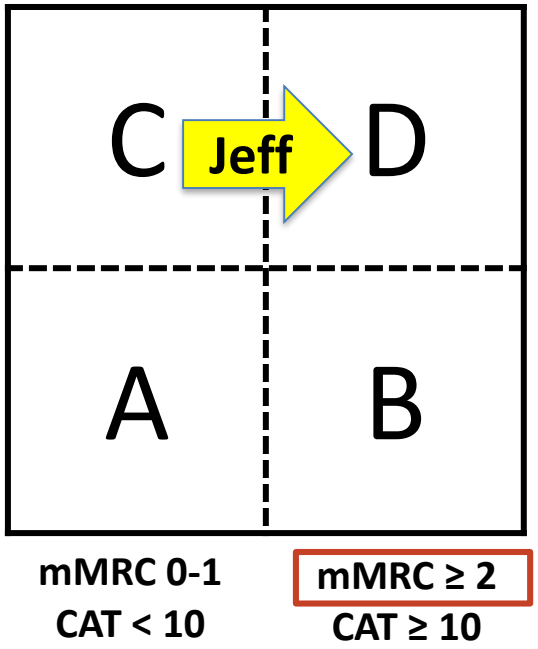
Jeff→ 0.54

	FEV_1 (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

Jeff→ 51% predicted

Moderate or severe exacerbation history

≥ 2 or ≥ 1 leading to hospital admission — 2
0 or 1 (not leading to hospital admission)



What Is the Next Step in Management for Jeff?

- ? Smoking cessation counseling
- ? Obtain 2D-Echo
- ? Refer to pulmonary rehab
- ? Assess need for oxygen therapy
- ? Step up therapy

Jeff: Next Steps

- ✓ Smoking cessation counseling
- ✓ Obtain 2D-Echo
- ✓ Refer to pulmonary rehab
- ✓ Assess need for oxygen therapy
- ✓ Step up therapy

Questions

- What is your treatment recommendation for Jeff?
- Does Jeff's blood eosinophil count affect your treatment choice?
- Do Jeff's comorbidities (cardiac disease, diabetes, history of pneumonia) affect your recommendations?
- Describe your plans for evaluating his inhaler technique
- What will you do if he has persistent symptoms or another exacerbation over the next 2 months?

➢MODIFIED MRC DYSPNEA SCALE[a]

PLEASE TICK THE BOX THAT APPLIED TO YOU

mMRC Grade 0.	I only get breathless with strenuous exercise	☐
mMRC Grade 1.	I get short of breath when hurrying on the level or walking up a slight hill.	☐
mMRC Grade 2.	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	☒
mMRC Grade 3.	I stop for breath after walking about 100 meters or after a few minutes on the level.	☐
mMRC Grade 4.	I am too breathless to leave the house or I am breathless when dressing or undressing.	☐

Jeff's Symptoms: COPD Assessment Test

I never cough	0 1 2 3 4 5	I cough all the time	2
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	3
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	2
When I walk up a hill or one flight of stairs, I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs, I am very breathless	4
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	2
I am confident leaving my home, despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	2
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	3
I have lots of energy	0 1 2 3 4 5	I have no energy at all	3

Total Score 21

Pharmacological Management: Key Points

- Pharmacological therapy can reduce COPD symptoms, reduce frequency and severity of exacerbations, and improve health status and exercise tolerance

Inhaler technique needs to be assessed regularly!

- Pharmacological treatment should be individualized and guided by:
  - Symptom severity
  - Risk of exacerbations
  - Side effects
  - Comorbidities
  - Drug availability and cost
  - Patient's response, preference and ability to use various devices

Peak Inspiratory Flow Rate: An Important Consideration in COPD

- Low PIFR may lead to reductions in medication reaching the lungs and lung deposition

PIFR	Drug Deposition
Low (<30 L/min)	Tends toward mouth/throat
High (>60 L/min)	More effectively reaches lungs

- Most DPI devices require a minimum PIFR of 30 L/min
- PIFR >60 L/min may help maximize drug delivery
  - Some COPD patients have problems achieving required PIFR through DPIs, but training is useful to help some exceed the minimum required rate with small improvements.
- Metered dose inhalers (MDIs) should be used

Al-Showair, et al. Respir Med. 2007;101(11):2395-401. Virchow J, et al. Respir Med. 2008;102(1):10-9.

Goals for Treatment of Stable COPD

REDUCE SYMPTOMS

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

REDUCE RISK

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

Don't Forget!

- **Identify and reduce risk factor exposure**
  - Smoking cessation
  - Efficient ventilation should be recommended
  - Advise patients to avoid continued exposures the potential irritants

Adapted from GOLD 2019 Report. http://goldcopd.org/

Long-Acting Combinations for COPD

LAMA/LABA	Dose and Inhalation Device
Once Daily	
Umeclidinium/vilanterol	62.5/25 µg (DPI)
Tiotropium/olodaterol	5/5 µg (SMI)
Twice Daily	
Glycopyrrolate/formoterol	18/9.6 µg (MDI)
Indacaterol/glycopyrrolate	27.5/15.6 µg (DPI)

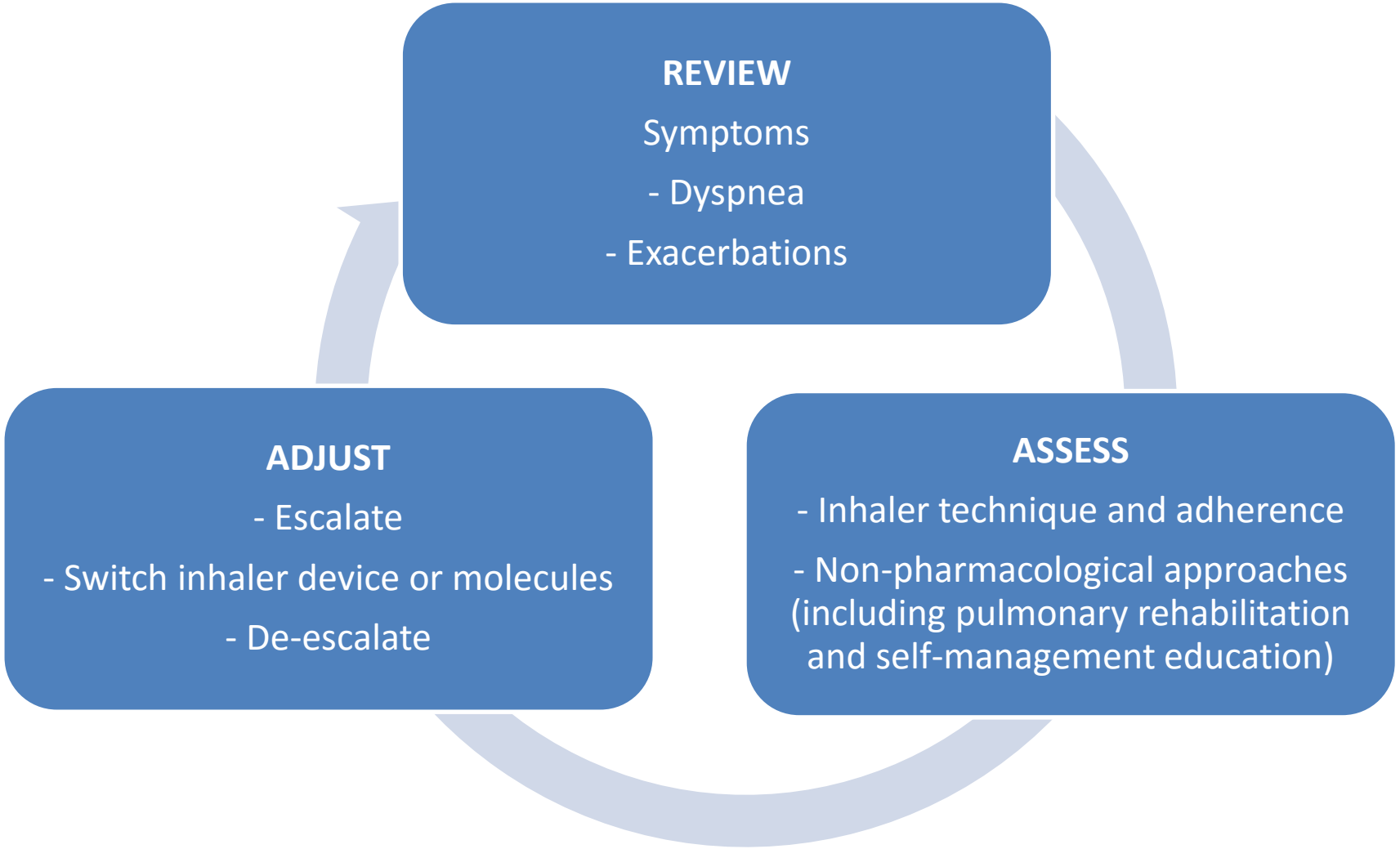
ICS/LAMA/LABA	Dose and Inhalation Device
Once Daily	
Fluticasone/umeclidinium/ vilanterol	100 µg/62.5/25 µg (DPI)

LABA/ICS	Dose and Inhalation Device
Once Daily	
Vilanterol/fluticasone furoate	25 µg/100 µg (DPI) daily
Twice Daily	
Formoterol/budesonide	4.5 µg/160 µg (MDI)
Formoterol/mometasone	5 µg/100 µg or 5 µg/200 µg (MDI)
Salmeterol/fluticasone	50 µg/250 µg (DPI)

Inhaled Therapies

- When a treatment is given by the inhaled route, the importance of education and training in inhaler device technique cannot be over-emphasized.
- The choice of inhaler device has to be individually tailored and will depend on access, cost prescriber, and most importantly, patient's ability and preference.
- It is essential to provide instructions and to demonstrate the proper inhalation technique when prescribing a device to ensure that inhaler technique is adequate and re-check at each visit that patients continue to use their inhaler correctly.
- Inhaler technique (and adherence to therapy) should be assessed before concluding that the current therapy is insufficient.

COPD Management Cycle



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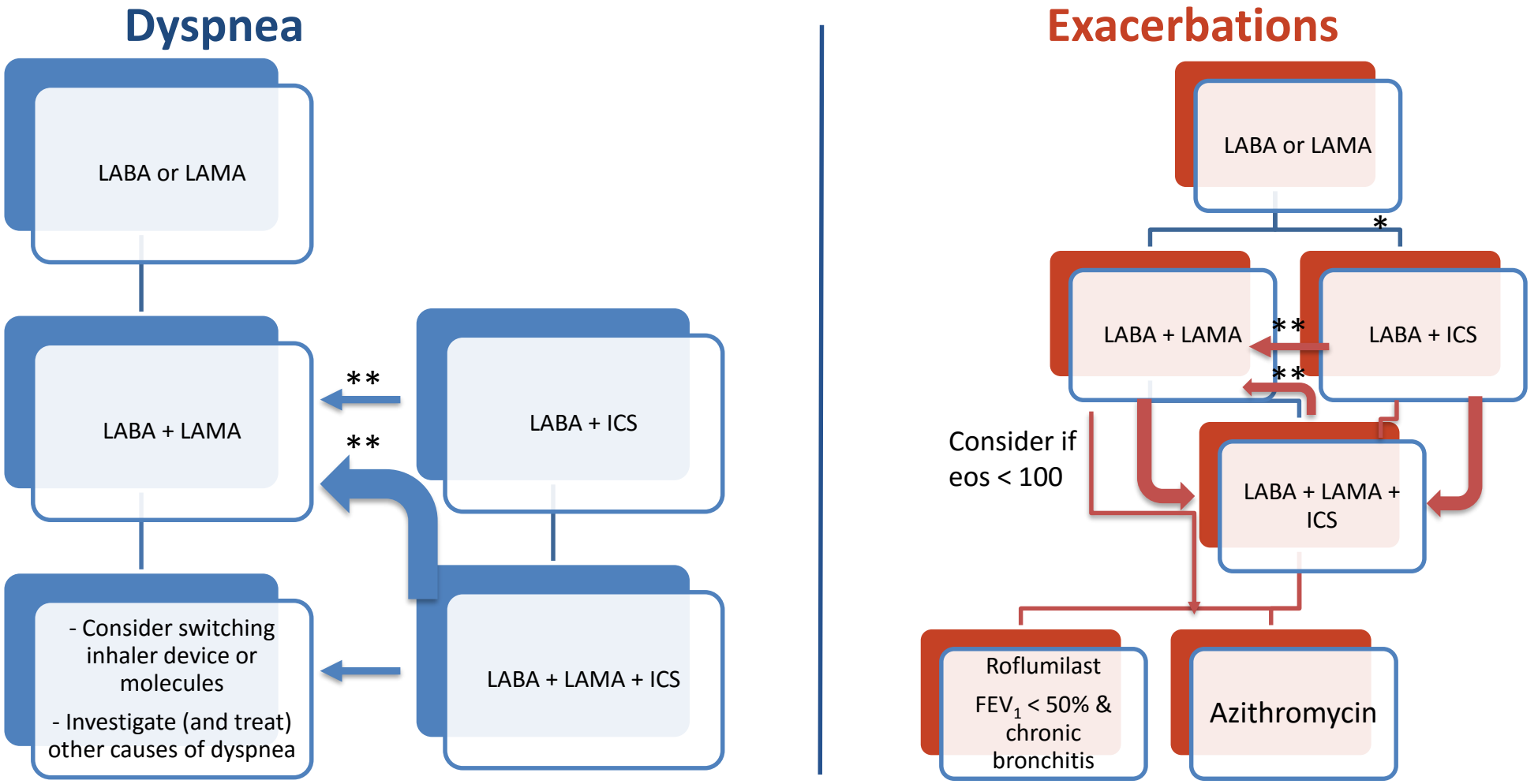
If Response to Treatment Is Not Adequate



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

Adapted from GOLD 2019 Report. http://goldcopd.org/

Non-Pharmacological Management: Key Points

- Patient education and self-management
- Influenza and pneumococcal vaccines decrease the incidence of lower respiratory tract infections
- Pulmonary rehabilitation improves symptoms, quality of life and physical/emotional participation in everyday activities
- In patients with severe resting chronic hypoxemia, long-term oxygen therapy improves survival
- Palliative approaches are effective in controlling symptoms in advanced COPD

Adapted from GOLD 2019 Report. http://goldcopd.org/