# Overview of COPD and Pulmonary Hypertension



Elyce T Sheehan, MD Assistant Professor Pulmonary and Critical Care University of New Mexico NMAFP Ruidoso, NM 8/3/2023

### Learning Objectives

- 1. Understand the definition, basic physiology, and diagnostic criteria for COPD
- 2. Understand the treatment options available for COPD
- 3. Understand the definition, basic physiology, and diagnostic criteria for pulmonary hypertension
- 4. Understand the treatment options available for pulmonary hypertension

## **Diagnosis of COPD**

#### **Compatible History**

#### **SYMPTOMS**

Shortness of breath Chronic cough Sputum production

#### EXPOSURE TO RISK FACTORS Tobacco Occupation Indoor/outdoor pollution

#### **Host Factors:**

Factors affecting lung growth Severe childhood asthma Genetic Factors/Family history Frequent childhood infections In utero exposures Pre-mature birth

#### **SPIROMETRY**

Martinez F, NEJM 2016; 375(9)871-8

#### A Word on Treatable Traits in COPD



Agusti, Eur Respir J 2016 47:410-419
van 't Hul, ERJ Open Res 2020; 6:00438-2020
van Dijk, ERJ Open Res 2020; 6:00322-2019
David, Thorax 2021;76:188-195.
Image from https://medium.com

#### Spirometry



### **GOLD** Criteria



#### Guide to Pharmacological Management



\*single inhaler therapy may be more convenient and effective than multiple inhalers Exacerbations refers to the number of exacerbations per year

### **Escalating Therapy**

#### DYSPNEA LABA or LAMA LABA + LAMA\* · Consider switching inhaler device or molecules Implement or escalate

non-pharmacologic treatment(s)

 Investigate (and treat) other causes of dyspnea





\*Single inhaler therapy may be more convenient and effective than multiple inhalers

\*\*Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood eos ≥ 300 cells/µl de-escalation is more likely to be associated with the development of exacerbations

Exacerbations refers to the number of exacerbations per year

#### A Promising Biomarker: Eosinophils

The Lancet Respiratory Medicine 2019

# Eosinophilic inflammation in COPD: from an inflammatory marker to a treatable trait

Benjamin David,<sup>1</sup> Mona Bafadhel <sup>(0)</sup>,<sup>2</sup> Leo Koenderman,<sup>3</sup> Antony De Soyza<sup>4</sup>

Thorax 2021



EUROPEAN RESPIRATORY journal

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

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### The Effect of Exacerbation History on Outcomes in the IMPACT Trial

David M.G. Halpin, Mark T. Dransfield, MeiLan K. Han, C. Elaine Jones, Sally Kilbride, Peter Lange, David A. Lipson, David A. Lomas, Fernando J. Martinez, Steve Pascoe, Dave Singh, Robert Wise, Gerard J. Criner

Blood eosinophils and treatment response with triple and dual combination therapy in chronic obstructive pulmonary disease: analysis of the IMPACT trial

Steven Pascoe, Neil Barnes, Guy Brusselle, Chris Compton, Gerard J Criner, Mark T Dransfield, David M G Halpin, MeiLan K Han, Benjamin Hartley, Peter Lange, Sally Lettis, David A Lipson, David A Lomas, Fernando J Martinez, Alberto Papi, Nicolas Roche, Ralf J P van der Valk, Robert Wise, Dave Singh

#### ORIGINAL ARTICLE 2020

#### Inhaled Steroids, Circulating Eosinophils, Chronic Airway Infection, and Pneumonia Risk in Chronic Obstructive Pulmonary Disease A Network Analysis

Miguel Angel Martinez-Garcia<sup>1</sup>, Rosa Faner<sup>2,3</sup>, Grace Oscullo<sup>1</sup>, David de la Rosa<sup>4</sup>\*, Juan-Jose Soler-Cataluña<sup>5</sup>, Marta Ballester<sup>6</sup>, and Alvar Agusti<sup>2,3,7</sup>

#### Triple therapy in COPD: The IMPACT trial

#### The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 3, 2018

VOL. 378 NO. 18

#### Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD

David A. Lipson, M.D., Frank Barnhart, D.V.M., Noushin Brealey, M.D., Jean Brooks, M.Sc., Gerard J. Criner, M.D., Nicola C. Day, Ph.D., Mark T. Dransfield, M.D., David M.G. Halpin, M.D., MeiLan K. Han, M.D., C. Elaine Jones, Ph.D., Sally Kilbride, M.Sc., Peter Lange, M.D., David A. Lomas, M.D., Ph.D., Fernando J. Martinez, M.D., Dave Singh, M.D., Maggie Tabberer, M.Sc., Robert A. Wise, M.D., and Steven J. Pascoe, M.B., B.S., for the IMPACT Investigators

Lipson D, N Engl J Med 2018;378:1671-80

### Triple therapy in COPD: The ETHOS trial

#### ORIGINAL ARTICLE

#### Reduced All-Cause Mortality in the ETHOS Trial of Budesonide/Glycopyrrolate/Formoterol for Chronic Obstructive Pulmonary Disease

A Randomized, Double-Blind, Multicenter, Parallel-Group Study

Fernando J. Martinez<sup>1\*</sup>, Klaus F. Rabe<sup>2\*</sup>, Gary T. Ferguson<sup>3</sup>, Jadwiga A. Wedzicha<sup>4\*</sup>, Dave Singh<sup>5</sup>, Chen Wang<sup>6</sup>, Kimberly Rossman<sup>7</sup>, Earl St. Rose<sup>7</sup>, Roopa Trivedi<sup>8</sup>, Shaila Ballal<sup>7</sup>, Patrick Darken<sup>9</sup>, Magnus Aurivillius<sup>10</sup>, Colin Reisner<sup>7</sup>, and Paul Dorinsky<sup>8</sup>; on behalf of the ETHOS Investigators

52-week, randomized, double-blind, trial of 8509 patients across 26 countries

Patients received either high-dose ICS/LABA/LAMA, low-dose ICS/LABA/LAMA, high-dose ICS/LABA, or LABA/LAMA

The ICS, LABA, and LAMA were different medications from IMPACT

Patients had a history of moderate or severe exacerbations within the year prior to enrollment

Triple therapy with both low dose and high dose ICS resulted in a lower rate of moderate or severe COPD exacerbations than LABA/LAMA or high-dose ICS/LABA.

Triple therapy with high-dose ICS reduced the risk of death compared with LABA/LAMA.

Rabe KF, N Engl J Med 2020; 383:35-48 Martinez FJ, AJRCCM 2020; 203(5): 553-564





tinez FJ, AJRCCM 2020; 203(5): 5

### **Risks of Inhaled Corticosteroids**

- Pneumonia<sup>1</sup> (RR, 1.59, 95% CI, 1.33-1.90)
- Tracheobronchomalacia<sup>2</sup>
- Non-tuberculous mycobacteria<sup>3</sup>
- Oral candidiasis
- Dysphonia
- Cataracts
- Possible systemic effects on bone health, glycemic control, adrenal suppression

Yang, Int Immunopharm 2019; 77:105950.
Shah, CHEST 2020;157(6):1426-1434
Brode, Eur Respir J 2017; 50:1700037.

#### Non-Pharmacologic Management

- Smoking Cessation
- Pulmonary Rehabilitation
- Oxygen Supplementation (Sa02 < 88% or Pa02 < 55)</p>
- Interventional (LVRS, Bullectomy, Bronchoscopic Interventions, Transplant)
- NIPPV (stable COPD w marked hypercapnia > 53mmHg)
- Vaccinations

### Closing thoughts on COPD...

- LABA+LAMA preferred over single agent
- When do you add an ICS?
  - History of, or concomitant, asthma
  - If recurrent exacerbations (Hospitalization (s) OR >/= 2 moderate exacerbations per year)
  - If blood eos >300 cells/ul
- When should you refer to pulmonary?

### Switching Gears...



#### What is Pulmonary Hypertension?

► The hemodynamic definition of PH has been updated as mPAP >20 mmHg.



#### **Group 1 - Pulmonary Arterial Hypertension**

- 1.1 Idiopathic
- 1.2 Heritable
- 1.3 Associated with drugs and toxins
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 HIV infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease
  - 1.4.5 Schistosomiasis
- 1.5 PAH with features of venous/capillary (PVOD/PCH) involvement
- 1.6 Persistent PH of the newborn









CO = cardiac output; NYHA = New York Heart Association functional class; PAP = pulmonary arterial pressure; PVR = pulmonary vascular resistance

#### Prognosis

- 1-yr incident mortality rate is 15% despite PAH therapy.
- Prognosis is worse in older pts and in PAH assoc. with scleroderma vs. IPAH.
- PAH assoc. with scleroderma has a 3-yr survival rate of 34% to 47%.

D'Alonzo et al. Ann Intern Med 1991;115:343-349.

Ghio et al. J Am Coll Cardiol 2001;37:183–188; 3. Oswald-Mamosser et al. Chest 1995;107:1193–1198; 4. Lettieri et al. Chest 2006;129:746–752; 5. Kunieda et al. Intern Med 1999;38:543–546.



# CLINICAL FEATURES: SYMPTOMS & SIGNS

#### **Symptoms**

- Dyspnea on exertion.
- Fatigue.
- Palpitations.
- Weight gain.
- Syncope.

#### Signs

- Distended and pulsating jugular veins.
- Abdominal distention.
- Hepatomegaly.
- Ascites.
- Peripheral edema.
- Accentuated P2 sounds.

Diagnosis should be focused on 2 tasks

- 1. Fast-track referral to PH centers in pts with a high likelihood of PAH, CTEPH, other forms of severe PH.
- Identifying underlying diseases, especially LHD (group 2 PH) and lung disease (group 3 PH), to ensure proper classification, and treatment.

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. European Heart Journal, ehac237, :26 August 2022.

### High Suspicion for PAH – Initial Workup

- Medical/Family Hx
- P/E (BP, HR, pulse ox, ambulatory sat if able)
- CMP for kidney, liver function, and electrolytes.
- Serologic testing for CTD, hepatitis, HIV.
- BNP/NTproBNP
- ECG

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. European Heart Journal, ehac237, :26 August 2022

Galie N et al. Eur Heart J. 2016; 37(1): 67-119.

Pulmonary hypertension RN. Blood tests. Available at http://pulmonaryhypertensionrn.com/blood-tests/.



#### Figure 1. Sample ECG with Signs of Pulmonary Hypertension

PAH, pulmonary arterial hypertension; RAD, right axis deviation; RVH, right ventricular hypertrophy; RV, right ventricle.

# High Suspicion for PAH – Step 2

#### <u>Step 2.</u>

Non-invasive lung and cardiac testing:

- Echocardiography
- Chest X-Ray
- \*PFTs
- \*V/Q Scan

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. European Heart Journal, ehac237, :26 August 2022.

### DIAGNOSIS OF PAH: ROLE OF CHEST X-RAY

#### Figure 1. Characteristic X-Ray of a Patient with PAH



## DIAGNOSIS OF PAH: ROLE OF TTE



# Role of PFTs

# Decreased DLCO and mild/moderate reduction in lung volumes usually seen in PAH.

In patients with systemic sclerosis:

 Reduced DLCO and normal lung volumes is suggestive of PAH.

Galie N, et al . Eur Respir J. 2015; 46:903-975.

McGoon M, et al. Chest. 2004; 126 (1 supp!): 14S-34S.

# ROLE OF V/Q SCAN

- >1 segmental –sized or larger mismatched perfusion defects seen with CTEPH.
- Normal V/Q scan makes CTEPH diagnosis unlikely.

Galie N, et al . Eur Respir J. 2015; 46:903-975.

McGoon M, et al. Chest. 2004; 126 (1 supp!): 14S-34S.



### High suspicion for PAH- Step 3

#### **Referral to a PH center for further evaluation:**

- When an intermediate/high probability of PH is established.
- In the presence of risk factors for PAH, or a history of PE.

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. European Heart Journal, ehac237, :26 August 2022.



# ROLE OF RHC

Required to confirm the diagnosis of PAH.

Excludes left sided heart disease, assesses CHD.

Measures response to vasodilator challenge.

Measures degree of R heart dysfunction (RAP, C0/CI).

Guides therapy for PAH.

Updated hemodynamic definition of PH: mPAP >20 mmHg. The definition also implies a PVR >2 WU and PAWP  $\leq$ 15 mmHg.

Galie N et al. Eur Heart J. 2016; 37(1): 67-119. McLaughlin W et al. J Am Coll Cardiol. 2009;53(17): 1573-1619.

### **RISK ASSESSMENT**

Determinants of prognosis	Low risk	Intermediate-low risk	Intermediate-high risk	High risk
Points assigned	1	2	3	4
WHO-FC	l or ll <sup>a</sup>	-	III	IV
6MWD, m	>440	320-440	165–319	<165
BNP or	<50	50–199	200–800	>800
NT-proBNP,ª ng/L	<300	300–649	650–1100	>1100



#### **Treatment of PAH**

- Treat the underlying cause
- Targeted therapies:

#### NITRIC OXIDE PATHWAY. Oral meds.

Sildenafil (Revatio, Viagra), Tadalafil (Adcirca), Riociguat (Adempas).

#### **PROSTACYLIN PATHWAY**. Oral, INH, SC, and IV

- Uptravi (oral) (Selexipag)
- Orenitram (oral), Tyvaso (inhaled) Remodulin (SC,IV) (Treprostinil)
- Ventavis (inhaled) (Iloprost)
- Flolan (IV), Veletri (IV) (Epoprostenol)

#### ENDOTHELIN PATHWAY. Oral meds.

Bosentan (Tracleer), Ambrisentan (Letairis), Macitentan. (Opsumit).

## GOALS OF THERAPY

- Improve FC, hemodynamic and TTE parameters.
- Improve exercise capacity and quality of life.
- Prevent disease progression.

Improve survival.

Barst RJ et al. J AM Coll Cardiol. 2009;54(1 Suppl): S78-S84. McLaughlin VV et al. J Am Coll Cardiol. 2013;62 (25 Suppl): D73-D81. McLaughlin VV et al. Circulation. 2009; 119: 2250–2294.

#### Common questions...

- Should I call pulmonary when the RV is enlarged on a CT scan?
- When should I get an echo?
- What if the echo says "pulmonary hypertension"?
- When should I refer to PH clinic?
- Other?

# Questions?

#### **COPD** References

- 1) Global Strategy for Prevention, Diagnosis and Management of COPD: 2023 Report
- 2) Martinez FD, et al. Early-Life Origins of Chronic Obstructive Pulmonary Disease. NEJM 2016; 375:871-878.
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### THANK YOU