Pulmonary Hypertension: A Patient-Centered, Team-based Approach to Optimizing Outcomes in PAH and CTEPH
Faculty

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Faculty Disclosures

- Consultant: Acceleron, Actelion, Gilead, Liquidia, Pfizer, United Therapeutics
- Grants to TMC: Acceleron, Actelion, Bayer, Complexa, Gilead, Liquidia, United Therapeutics
Learning Objectives

- Identify strategies to screen and improve early recognition of pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH)
- Apply guideline recommendations to the accurate diagnosis of PAH and CTEPH
- Develop a guideline-directed, evidence-based management plan for PAH and CTEPH that includes consideration of novel therapies and current clinical trial data
- Establish a multidisciplinary, patient-centered approach to care for patients with PAH or CTEPH
Introduction
WHO Classification Groups

Group 1
PAH

Group 2
PH due to Left Heart Disease

Group 3
PH due to Lung Disease or Hypoxia

Group 4
CTEPH

Group 5
PH with Unclear Multifactorial Mechanisms

PAH & CTEPH:
mPAP >25 mmHg
PAWP <15 mmHg
PVR >3 Wood units

CTEPH Only:
Emboli in pulmonary arteries

ESC/ERS, European Society of Cardiology/European Respiratory Society; mPAP, mean pulmonary arterial pressure; PAWP, pulmonary arterial wedge pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; WHO, World Health Organization.

PAH Group I

- Idiopathic (IPAH)
- Hereditary (HPAH)
- Associated with (APAH)
  - Collagen vascular disease
  - Congenital systemic-to-pulmonary shunts
  - Portal hypertension
  - HIV infection
  - Drugs/toxins

- Persistent pulmonary hypertension of the newborn
- Associated with venous or capillary involvement
  - Pulmonary veno-occlusive disease (PVOD)
  - Pulmonary capillary hemangiomatosis (PCH)
Right-sided Heart Failure
Early Recognition of PAH and CTEPH
Diagnosed Patients: Age Distribution & Prevalence

**PAH vs CTEPH**
- **PAH**: 15 cases per million adults
- **CTEPH**: 3.2 cases per million adults

WHO Functional Classes: PAH & CTEPH

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>No limitation of usual physical activity; ordinary physical activity does not cause increased dyspnea, fatigue, chest pain, or presyncope.</td>
</tr>
<tr>
<td>II</td>
<td>Mild limitation of physical activity. There is no discomfort at rest, but normal physical activity causes increased dyspnea, fatigue, chest pain, or presyncope.</td>
</tr>
<tr>
<td>III</td>
<td>Marked limitation of physical activity. There is no discomfort at rest, but less than normal physical activity causes increased dyspnea, fatigue, chest pain, or presyncope.</td>
</tr>
<tr>
<td>IV</td>
<td>Unable to perform any physical activity at rest and may have signs of right ventricular (RV) failure. Dyspnea and/or fatigue may be present at rest, and symptoms are increased by almost any physical activity.</td>
</tr>
</tbody>
</table>

Importance of Early Recognition

![Graph showing survival rates for different types of PAH](chart)

**Survival**
- **PAH**
- **APAH-Other**
- **APAH-CHD**
- **IPAH/HPAH**
- **APAH-CTD**

**Follow-up Years**
- 100%
- 81%
- 73%
- 64%
- 31%
- 25%
- 17%

**Screened**
- Routine practice

- CHD, congenital heart disease; CTD, connective tissue disease; SSc, systemic sclerosis.
Importance of Early Recognition (cont’d)

- CTEPH is only PH with potential cure
- Pulmonary endarterectomy (PEA)
  - 20%-40% are inoperable
  - 80%-90% cured with PEA
  - Procedure mortality
    - In-hospital mortality: 4.7%
    - 1-year postoperative mortality: 7%

PAH Screening: ESC/ERS Recommendations

Symptoms of PH
Initial: Nonspecific, RV dysfunction
- Dyspnea
- Fatigue
- Weakness
- Angina
Later: Progressive RV failure

PAH
- Resting echocardiogram
  - 1° relatives of HPAH
  - PoPH: liver transplant
- Annual echocardiogram
  - 1° relatives of HPAH
  - PAH mutation +
- Exercise echocardiogram not recommended in high-risk patients

SSc-PAH (APAH-CTD)
- Resting echocardiogram
  - Asymptomatic patients
- Combined approach
- Annual screening
  - Echocardiograph, PFTs, biomarkers
- mPAP 21-24 mmHg
- DETECT algorithm
  - >3 years disease
  - DLCO <60% predicted

DLCO, diffusing lung capacity for carbon monoxide; PFT, pulmonary function test; PoPH, portopulmonary hypertension; RV, right ventricular.

Screening for CTEPH

Risk Factors for CTEPH

- History of pulmonary embolism (PE)
- Right-sided heart strain at initial PE
- Hypercoagulable states
  - Elevated factor VIII
  - Factor V Leiden mutation
  - Lupus
- Splenectomy
- Hypothyroidism
- Chronic inflammation
- History of malignancy
- Ventriculoarterial shunts or pacemakers
- Unexplained PH

Incidence after acute PE: 0.5% to 9%
History of acute PE in diagnosed: 75%

Diagnosis of PAH and CTEPH
Diagnostic Algorithm: ESC/ERS Guidelines

1. **Symptoms, signs, history suggestive of PH**
   - Determine echocardiographic probability of PH
     - **High or intermediate**
       - Consider left heart disease and lung disease by symptoms, signs, risk factors, ECG, PFT+DLCO, choix radiograph and HRCT, arterial blood gases
         - **Yes**
           - Diagnosis of left heart disease or lung disease confirmed?
             - No sign of severe PH/RV dysfunction
               - No
               - Treat underlying disease
             - Signs of severe PH/RV dysfunction
               - **Yes**
                 - Refer to PH expert center
               - **No**
                 - V/Q Scan
                   - Mismatched perfusion defects?
                     - No

2. **Low**
   - Consider other causes and/or follow-up

V/Q Scan

Ventilation Perfusion

Normal or Mottled Pattern

PAH

CTEPH

At least one segmental perfusion defect inconsistent with ventilation scan findings

CTEPH possible: CT pulmonary angiography, RHC +/- pulmonary angiography

PAH likely
Specific diagnostic tests

CTD
Drugs - Toxin
HIV

CTD

CHD
PoPH
Schistosomiasis

Mean pulmonary artery pressure (mPAP) of ≥25 mmHg at rest

AND

Mean pulmonary capillary wedge pressure (PCWP) of <15 mmHg

(No evidence of left-heart disease)

PVR >3 Wood units

- Most PH cases are not in WHO group I!!!
- **PAH**
  - ↑PVR
  - ↑Transpulmonary pressure gradient (TPG)
  - Normal left-sided filling pressures
- Pulmonary venous hypertension (**PVH**) characterized by
  - ↑PCWP, usually normal TPG, and PVR
Therapy for PAH
Targeting Multiple Pathologic Pathways Improves Response

## Goals of Treatment in 2018: Improvement to a Goal

- **However…** *improvement* and *normalization* of **ALL clinical parameters** to make patients **LOW RISK** is the goal in PAH treatment
- **Preservation or prevention of worsening** is no longer the goal

<table>
<thead>
<tr>
<th>Determinants of Prognosis (estimated 1-year mortality)</th>
<th>Low Risk (&lt;5%) AT GOAL!!!</th>
<th>Intermediate Risk (5-10%) NOT AT GOAL</th>
<th>High Risk (&gt;10%) NOT AT GOAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs of right heart failure</td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Progression of symptoms</td>
<td>No</td>
<td>Slow</td>
<td>Rapid</td>
</tr>
<tr>
<td>Syncope</td>
<td>No</td>
<td>Occasional syncope</td>
<td>Repeated syncope</td>
</tr>
<tr>
<td>WHO Functional Class</td>
<td>I, II</td>
<td>III</td>
<td>IV</td>
</tr>
<tr>
<td>6MWD</td>
<td>&gt;440 m</td>
<td>165-440 m</td>
<td>&lt;165 m</td>
</tr>
<tr>
<td>Cardiopulmonary exercise testing</td>
<td>Peak VO$_2$ &gt;15 mL/min/kg (&gt;65% predicted) VE/VCO$_2$ slope &lt;36</td>
<td>Peak VO$_2$ 11-15 mL/min/kg (35%-65% predicted) VE/VCO$_2$ slope 36-44.9</td>
<td>Peak VO$_2$ &lt;11 mL/min/kg (&lt;35% predicted) VE/VCO$_2$ slope ≥45</td>
</tr>
<tr>
<td>NT-proBNP levels</td>
<td>BNP &lt;50 ng/L</td>
<td>BNP 50-300 ng/L</td>
<td>BNP &gt;300 ng/L</td>
</tr>
<tr>
<td></td>
<td>NT-pro BNP &lt;300 ng/L</td>
<td>NT-pro BNP 300-1400 ng/L</td>
<td>NT-pro BNP &gt;1400 ng/L</td>
</tr>
<tr>
<td>Imaging (ECHO or CMR)</td>
<td>RA area &lt;18 cm$^2$</td>
<td>RA area 18-26 cm$^2$</td>
<td>RA area &gt;26 cm$^2$</td>
</tr>
<tr>
<td></td>
<td>No pericardial effusion</td>
<td>No/minimal pericardial effusion</td>
<td>Pericardial effusion</td>
</tr>
<tr>
<td>Hemodynamics</td>
<td>RAP &lt;8 mmHg Cl ≥2.5 L/min/m$^2$ SvO$_2$ &gt; 65%</td>
<td>RAP 8-14 mmHg Cl 2.0-2.4 L/min/m$^2$ SvO$_2$ 60%-65%</td>
<td>RAP &gt;14 mmHg Cl &lt;2.0 L/min/m$^2$ SvO$_2$ &lt;60%</td>
</tr>
</tbody>
</table>

6MWD, 6-minute walk distance; CI, pulmonary clearance; CMR, cardiovascular magnetic resonance; NT-pro BNP, N-terminal pro-B-type brain natriuretic peptide; RA, right atrial; RAP, right atrial pressure; SVO$_2$, mixed venous oxygen saturation; VE/VCO$_2$, ventilation:carbon dioxide output; VO$_2$, peak oxygen uptake.

## Drug Monotherapy
### Medications for PAH: ESC/ERS Guidelines

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class - Level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WHO FC II</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>I</td>
</tr>
<tr>
<td>Endothelin receptor antagonists (ERA)</td>
<td>I</td>
</tr>
<tr>
<td>Ambrisentan</td>
<td>I</td>
</tr>
<tr>
<td>Bosentan</td>
<td>I</td>
</tr>
<tr>
<td>Macitentan — NOVEL AGENT</td>
<td>IIb</td>
</tr>
<tr>
<td>Phosphodiesterase type-5 inhibitors (PDE-5i)</td>
<td>C</td>
</tr>
<tr>
<td>Sildenafil</td>
<td>I</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>I</td>
</tr>
<tr>
<td>Vardenafil*</td>
<td>IIb</td>
</tr>
<tr>
<td>Guanylate cyclase stimulators</td>
<td>I</td>
</tr>
<tr>
<td>Riociguat — NOVEL AGENT</td>
<td>I</td>
</tr>
<tr>
<td>Prostacyclin analogues</td>
<td>—</td>
</tr>
<tr>
<td>Epoprostenol</td>
<td>—</td>
</tr>
<tr>
<td>Iloprost</td>
<td>—</td>
</tr>
<tr>
<td>IV*</td>
<td>—</td>
</tr>
<tr>
<td>Treprostinil</td>
<td>—</td>
</tr>
<tr>
<td>Subcutaneous (SC)</td>
<td>—</td>
</tr>
<tr>
<td>Inhaled</td>
<td>—</td>
</tr>
<tr>
<td>IV</td>
<td>—</td>
</tr>
<tr>
<td>Oral</td>
<td>—</td>
</tr>
<tr>
<td>Beraprost*</td>
<td>—</td>
</tr>
<tr>
<td>Prostacyclin receptor (IP) agonists</td>
<td>I</td>
</tr>
<tr>
<td>Selexipag (oral) — NOVEL AGENT</td>
<td>I</td>
</tr>
</tbody>
</table>

*Included in recommendations but not yet approved for PAH indication

FC, functional class.
## Initial Combination Therapy Medications for PAH: ESC/ERS Guidelines

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class - Level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WHO FC II</td>
</tr>
<tr>
<td>Ambrisentan + tadalafil</td>
<td>I</td>
</tr>
<tr>
<td>Other ERA + PDE-5i</td>
<td>Ila</td>
</tr>
<tr>
<td>Bosentan + sildenafil + IV epoprostenol</td>
<td>—</td>
</tr>
<tr>
<td>Bosentan + IV epoprostenol</td>
<td>—</td>
</tr>
<tr>
<td>Other ERA or PDE-5i + SC treprostinil</td>
<td>—</td>
</tr>
<tr>
<td>Other ERA or PDE-5i + other IV prostacyclin analogues</td>
<td>—</td>
</tr>
</tbody>
</table>

## Sequential Combination Therapy
### Medications for PAH: ESC/ERS Guidelines

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class - Level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WHO FC II</td>
</tr>
<tr>
<td>Macitentan added to sildenafil</td>
<td>I</td>
</tr>
<tr>
<td>Riociguat added to bosentan</td>
<td>I</td>
</tr>
<tr>
<td>Selexipag added to ERA and/or PDE-5i</td>
<td>I</td>
</tr>
<tr>
<td>Sildenafil added to epoprostenol</td>
<td>—</td>
</tr>
<tr>
<td>Treprostinil inhaled added to sildenafil or bosentan</td>
<td>Ia</td>
</tr>
<tr>
<td>Iloprost inhaled added to bosentan</td>
<td>Ia</td>
</tr>
<tr>
<td>Tadalafil added to bosentan</td>
<td>Ila</td>
</tr>
<tr>
<td>Ambrisentan added to sildenafil</td>
<td>Ila</td>
</tr>
<tr>
<td>Bosentan added to epoprostenol</td>
<td>—</td>
</tr>
<tr>
<td>Bosentan added to sildenafil</td>
<td>Ila</td>
</tr>
<tr>
<td>Sildenafil added to bosentan</td>
<td>Ila</td>
</tr>
<tr>
<td>Other double combinations</td>
<td>Ila</td>
</tr>
<tr>
<td>Other triple combinations</td>
<td>Ila</td>
</tr>
<tr>
<td>Riociguat added to sildenafil or other PDE-5i</td>
<td>III</td>
</tr>
</tbody>
</table>

PAH Treatment Algorithm: ESC/ERS Guidelines

- Treatment-Naive Patient
  - CCB Therapy
    - Acute Vasoreactivity Test (IPAH/HPAH/DPAH only)
      - PAH Confirmed by Expert Center
        - Vasoreactive
          - Monotherapy
          - Oral Combo
            - Low or Intermediate Risk (WHO FC II-III)
              - Inadequate Clinical Response
                - Double or Triple Sequential Combination
                  - Inadequate Clinical Response
                    - Consider Lung Transplantation
            - Non-vasoreactive
              - High Risk (WHO FC IV)
                - Combo incl. IV PCA

- Patient Already on Treatment

CCB, calcium channel blocker; PCA, patient-controlled analgesia.
The AMBITION Trial: Evidence for Combination Therapy

Macitentan: SERAPHIN Trial
Novel Agent for PAH

- Change in Mean 6MWD by 6 Months
  - 10 mg: HR 0.55, 97.5% CI 0.39-0.76, P<.001
  - 3 mg: HR 0.70, 97.5% CI 0.52-0.96, P=.01

- Adverse Events
  - Worsening PAH: 30%, 22%, 35%
  - Upper resp. tract infect.: 20%, 15%, 13%
  - Peripheral edema: 16%, 18%, 18%
  - Nasopharyngitis: 15%, 14%, 10%
  - RV failure: 15%, 13%, 23%
  - Headache: 13%, 14%, 9%

- Patients without an Event (%)

Riociguat: PATENT Trials
Novel Agent for PAH

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>1.5 mg max (n=63)</th>
<th>2.5 mg max (n=254)</th>
<th>Placebo (n=126)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>32%</td>
<td>27%</td>
<td>20%</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>13%</td>
<td>19%</td>
<td>8%</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>22%</td>
<td>17%</td>
<td>11%</td>
</tr>
<tr>
<td>Nausea</td>
<td>16%</td>
<td>16%</td>
<td>13%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>24%</td>
<td>16%</td>
<td>12%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10%</td>
<td>14%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Selexipag: GRIPHON Trial
Novel Agent for PAH

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Selexipag (n=575)</th>
<th>Placebo (n=577)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>65%</td>
<td>33%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>42%</td>
<td>19%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Nausea</td>
<td>34%</td>
<td>19%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pain in jaw</td>
<td>26%</td>
<td>6%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Worsening of PAH</td>
<td>22%</td>
<td>36%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Vomiting</td>
<td>18%</td>
<td>9%</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

The TRITON Trial
Evidence for Combination Therapy

- The Efficacy and Safety of Initial Triple Versus Initial Dual Oral Combination Therapy in Patients With Newly Diagnosed Pulmonary Arterial Hypertension (TRITON)
Therapy for CTEPH
CTEPH Treatment Algorithm: ESC/ERS Guidelines

- Diagnosis Confirmed by CTEPH Expert Center
- Lifelong Anticoagulation
- Operability Assessment by a multidisciplinary CTEPH team
- Technically Operable
- Acceptable Risk/Benefit Ratio
- PEA
- Non-acceptable Risk/Benefit Ratio
- Persistent Symptomatic PH
- Targeted Medical Therapy
- Persistent Severe Symptomatic PH
- Consider BPA in Expert Center
- Consider Lung Transplantation

PEA Procedure (cont’d)

This shows how the scar tissue is removed from the artery wall (seen from the side).

© UHN Patient Education

Riociguat: CHEST-1 & CHEST-2 Trials
CTEPH Targeted Medical Therapy: ESC/ERS Guidelines

Mean Change in 6MWD

- Former Riociguat
- Former Placebo

Change in WHO FC

- Improved
- Stabilized
- Worsened

Importance of a Team-based, Patient-centered Approach to Care
Multidisciplinary Team

- Cardiologist
- Pulmonologist
- Clinical Nurse Specialist
- Radiologist
- Psychologist
- Social Worker
- Gastroenterologist
- Infectious Disease Specialist
- Rheumatologist

Referral center should have direct links and quick referral patterns to additional services

- CTD
- Family Planning
- PEA
- Transplant Center
- Adult CHD services
Palliative Care: Patient Perspectives from a Cross-sectional Survey

## Palliative Care: Physician Perspectives from a Cross-sectional Survey

### Reasons for Referral to PC

<table>
<thead>
<tr>
<th>Reason</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of life/active dying</td>
<td>59%</td>
</tr>
<tr>
<td>Hospice referral</td>
<td>46%</td>
</tr>
<tr>
<td>Dyspnea management</td>
<td>39%</td>
</tr>
<tr>
<td>Impaired quality of life</td>
<td>39%</td>
</tr>
<tr>
<td>Goals-of-care discussion</td>
<td>32%</td>
</tr>
<tr>
<td>Pain management</td>
<td>25%</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>14%</td>
</tr>
</tbody>
</table>

### Perceived Barriers to Referral

<table>
<thead>
<tr>
<th>Barrier</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient/Family not agreeable to consultation</td>
<td>51%</td>
</tr>
<tr>
<td>Patient will view as “giving up hope”</td>
<td>43%</td>
</tr>
<tr>
<td>Physician believes PC unnecessary</td>
<td>36%</td>
</tr>
<tr>
<td>Believes patients not eligible</td>
<td>28%</td>
</tr>
<tr>
<td>Gets in the way of PAH treatment</td>
<td>20%</td>
</tr>
<tr>
<td>“Palliative” has negative connotation</td>
<td>17%</td>
</tr>
<tr>
<td>Same as hospice and patient not ready</td>
<td>6%</td>
</tr>
</tbody>
</table>

PC, palliative care.
Addressing Adherence Issues

- Patient-centered care
- Self-efficacy is KEY
- Awareness of limitations in older patients
- Help with low health literacy
  - Simple language
  - Larger font sizes
  - Pictures/diagrams
Nurse-specific Training

- IV prostacyclin therapy
  - Medication orders
  - IV access
  - Initiation of therapy
  - Safety measures
  - Catheter priming for concentration changes or line changes
  - Pump management and maintenance
  - Care of central line and patient education

- Transitioning from one IV prostacyclin to another
Resources for Patients & Caregivers

- PHA association: www.phassociation.org
  - Resources for patients
  - Resources for clinicians
  - Clinical research
Case Evaluation
Case Evaluation: Patient Description

- 58-year-old female with scleroderma (>10 years)
- Evidence of progressive dyspnea over the preceding 6 months
- NYHA FC III
- Comorbidities
  - Smoker (>40 years)
  - Cough
  - Raynaud’s syndrome (>9 years)
- Cool extremities with evidence of peripheral edema
- Pansystolic murmur indicating tricuspid regurgitation

NYHA FC: New York Heart Association functional class.
The CXR

Peripheral Hypovascularity

Prominent Central Pulmonary Artery

Right Descending Pulmonary Artery

RV Enlargement

CXR, chest X-ray.
Irrespective of the pressure measurement, this heart is highly suspicious for PAH, based on structural changes.

LA=left atrium/atrial
LV=left ventricle/ventricular
RA=right atrium/atrial
RV=right ventricle/ventricular

Pericardial effusion
Our Patient’s Initial Test Results

- DLCO 54%
- FVC%/DLC%=1.7
- 6MWD=268 meters
- CXR reveals enlarged cardiac silhouette
- Right Heart Catheterization
  - mRAP: 12 mmHg
  - mPAP: 45 mmHg
  - CI: 2.3 L/min/m²
  - PVR: 12 Wood units

How would you treat this patient?
Goals of Treatment in 2018

- NYHA Functional Class is an important predictor of survival
- If PAH therapy is effective, improvement in NYHA FC from FC III/IV to FC II is consistent with improved PAH prognosis

<table>
<thead>
<tr>
<th>Variables Used in Clinical Practice to Determine Responses to Therapy and Prognosis in PAH Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional class</td>
</tr>
<tr>
<td>Echocardiography</td>
</tr>
<tr>
<td>Hemodynamics</td>
</tr>
<tr>
<td>6MWD</td>
</tr>
<tr>
<td>Cardiopulmonary exercise testing</td>
</tr>
<tr>
<td>B-type natriuretic peptide levels</td>
</tr>
</tbody>
</table>

EqCO₂, ventilatory equivalent for carbon dioxide.
What is the initial therapy for a high risk patient with Group I PAH (Functional Class II-III)?

A. Oral monotherapy
B. Oral dual combination therapy
C. IV infusion prostacyclin therapy
PAH and CTEPH are chronic, life-threatening conditions
- Require early recognition and accurate diagnosis

Diagnosis
- V/Q scan important to distinguish between PAH and CTEPH

Complex therapeutic management
- Guideline recommendations
- Novel therapies

Multidisciplinary, patient-centered approach is critical
- PH referral centers
- Cardiologists and pulmonologists
- Adherence issues
- High level of nursing competency
Clinical Pearls

- **Diagnosis**
  - Chest X-ray is inferior to ECG in diagnosing PAH
  - Structural changes may indicate PAH irrespective of pressure

- **Treatment**
  - PAH: Combination therapy is currently the standard of care
    - Targeting multiple pathways improves therapeutic response
    - Goal: Improvement and normalization to make patients LOW RISK
  - CTEPH: Patients ineligible for PEA should receive riociguat

- **Patient resources are important to ensuring outcomes!**
Questions and Answers
Thank You!