Addressing Diagnostic and Therapeutic Challenges in Pulmonary Arterial Hypertension through Pharmacist Intervention

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Disclosures

Dr. Jennings: Has nothing to disclose in relation to this presentation

This continuing medical education activity includes device brand names for participant clarity purposes only, due to the presence of different branded versions of the same device. No product promotion or recommendation should be inferred.

Learning Objectives

- Recognize the barriers to a timely PAH diagnosis and the clinical and socioeconomic impact of diagnostic delays
- Outline the diversity of PAH pathophysiologic mechanisms, therapeutic targets, and patient types with respect to impact on clinical outcomes and therapeutic design
- Evaluate traditional and newer approaches to the management of PAH with respect to their mechanisms of action, efficacy, safety, indications, and appropriate use across patient populations
- Employ pharmacy practice strategies to optimize the long-term management of PAH through informed, individualized, and coordinated care

PAH = pulmonary arterial hypertension.

Patient Case

- HL is a 43-year-old mother of three who presented with a 2-month history of dyspnea on exertion and fatigue consistent with class II to class III symptoms
- She reports a 1-year use of phentermine for weight loss prior to symptom onset
- She also reports that her mother had PAH and died at the age of 47 years
- She was diagnosed with PAH (heritable vs drug-induced) based on RHC

RHC = right heart catheterization.

Definition of PH vs PAH

Right Heart Catheterization Confirmed		Diagnosis
Increased mPAP	≥25 mm Hg	PH
Increased mPAP AND Normal PCWP	≥25 mm Hg <15 mm Hg	PAH

mPAP = mean pulmonary arterial pressure; PCWP = pulmonary capillary wedge pressure; PH = pulmonary hypertension.
Simonneau G, et al. *J Am Coll Cardiol.* 2013;62;D34-D41.

Clinical Classification

1. PAH
- Idiopathic PAH
- Heritable
- Drug and toxin-induced
- Associated with:
  - Connective tissue disorders
  - Human immunodeficiency virus infection
  - Portal hypertension
  - Congenital heart disease
  - Schistosomiasis

1'. Pulmonary Veno-Occlusive Disease (PVOD)

1". Persistent PH of Newborn

2. PH Owing to Left Heart Disease
- Left ventricular systolic dysfunction
- Left ventricular diastolic dysfunction
- Valvular disease
- Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

3. PH Owing to Lung Diseases and/or Hypoxia
- Chronic obstructive pulmonary disease
- Interstitial lung disease
- Other pulmonary diseases with mixed restrictive and obstructive pattern
- Sleep-disordered breathing
- Alveolar hypoventilation disorders
- Chronic exposure to high altitude
- Developmental abnormalities

4. Chronic Thromboembolic PH (CTEPH)

5. PH with Unclear Multifactorial Mechanisms
- Hematologic disorders (including chronic hemolytic anemia)
- Systemic disorders
- Metabolic disorders
- Others

Simonneau G, et al. *J Am Coll Cardiol.* 2013;62;D34-D41.

Drug- and Toxin-Induced PAH

Definite	Possible
• Aminorex • Fenfluramine • Dexfenfluramine • Toxic rapeseed oil • Benfluorex • SSRIs	• Cocaine • Phenylpropanolamine • St. John's wort • Chemotherapeutic agents • Interferon-α or -β • Amphetamine-like drugs
Likely	**Unlikely**
• Amphetamines • L-Tryptophan • Methamphetamines • Dasatinib	• Oral contraceptives • Estrogen • Cigarette smoking

SSRI = selective serotonin reuptake inhibitor.
Simonneau G, et al. *J Am Coll Cardiol.* 2013;62;D34-D41.

Epidemiology

- WHO group 1
- Incidence: 15 per million people
- Demographics
  - Mean age, 50 ± 14 years
  - 80% female
- 56% have symptoms with minimal activity or at rest
- Delay from symptom onset to diagnosis: 27 months

WHO = World Health Organization.
McGoon MD, et al. *J Am Coll Cardiol.* 2013;62:D51-59. McLaughlin VV, et al. *J Am Coll Cardiol.* 2015;65:1976-1997.

Functional Classification

WHO

- **Class I:** Symptoms elicited at levels of exertion that would limit normal individuals
- **Class II:** Symptoms on ordinary exertion
- **Class III:** Symptoms on less-than-ordinary exertion
- **Class IV:** Symptoms at rest

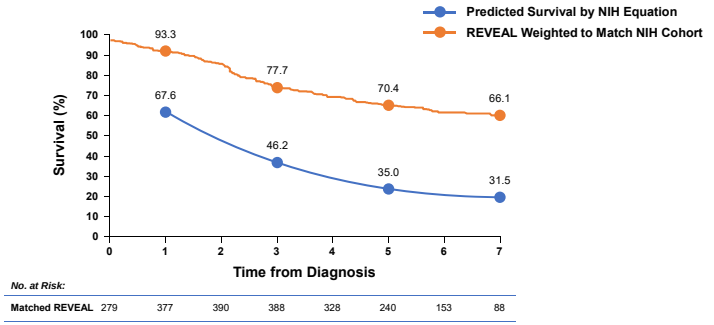
Pulmonaryfunctionrn.com. Functional classification of pulmonary hypertension. Four functional classes of pulmonary hypertension. http://pulmonaryhypertensionrn.com/functional-classification-of-pulmonary-arterial-hypertension-pah/. Accessed February 23, 2017.
Mathier MA. Medscape Education. 2006;10:2. http://www.medscape.org/viewarticle/544175. Accessed February 23, 2017.

Clinical Presentation

Common Initial Symptom	Patients (%)
Dyspnea	60
Fatigue	19
Syncope	13
Chest pain	7
Palpitations	5
Leg edema	3

McGoon M, et al. *Chest.* 2004;126:14S-34S.

REVEAL Registry: Survival



REVEAL = Registry to Evaluate Early And Long-term pulmonary arterial hypertension disease management; NIH = National Institutes of Health.
Benza RL, et al. *Chest.* 2012;142:448-456.

Risk Assessment

- **Low risk**
  - No RV failure
  - Gradual symptom progression
  - WHO FC II, III
  - Peak VO_2 >10.4 mL/min/kg
  - Minimal BNP elevation
  - Preserved cardiac index
- **High risk**
  - Evidence of RV failure
  - Rapid symptom progression
  - WHO FC IV
  - Peak VO_2 <10.4 mL/min/kg
  - Significant BNP elevation
  - Low cardiac index

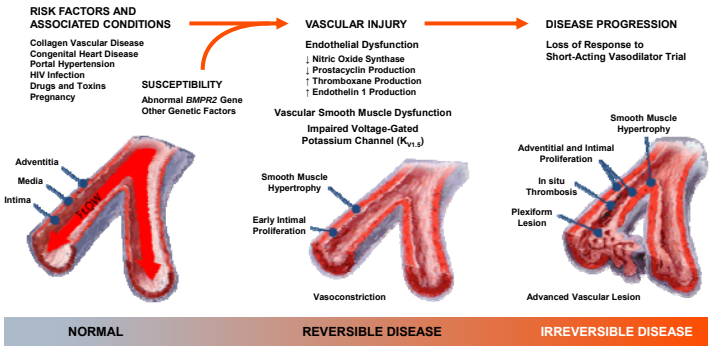
RV = right ventricular; BNP = brain natriuretic peptide; FC = functional classification.
McLaughlin VV, et al. *J Am Coll Cardiol*. 2009;53:1573-1619.

Hospitalizations and Costs

- Hospitalization for worsening PAH
  - Associated with poor prognosis
  - Costly
- Hospitalization costs greatly exceed pharmacy costs
  - Average costs of initial PAH-related hospitalization nearly $40,000
  - Post-initial hospitalization, subsequent admissions result in longer, more expensive stays
- Total healthcare costs: ~$8000 per-patient-per-month

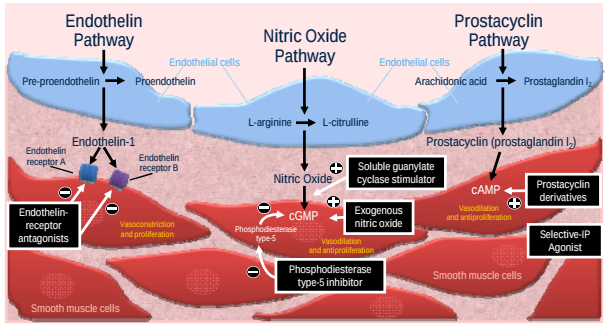
Campo A, et al. *Eur Respir J*. 2011;38:359-367. Sikirica M, et al. *BMC Health Services Research*. 2014;14:676. Burke JP, et al. *Am J Managed Care*. 2015;21:S47-S58. Galiè N, et al. *J Am Coll Cardiol*. 2013;62:D60-D72.

Pathogenesis



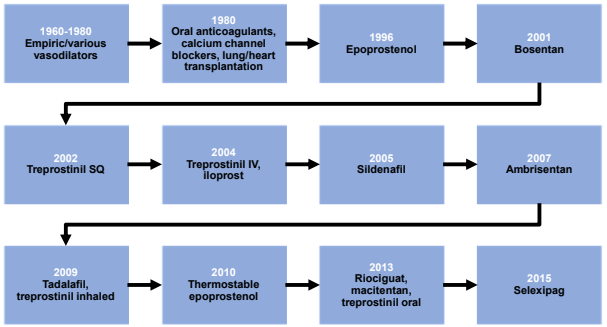
Gaine S. *JAMA*. 2000;284(24):3160-3168.

Therapeutic Targets



cGMP = cyclic guanosine monophosphate; cAMP = cyclic adenosine monophosphate.
Humbert M, et al. *N Engl J Med*. 2004;351:1425-1436.

Pharmacotherapy Timeline



SQ = subcutaneous; IV = intravenous.

Treatment Goals

- WHO FC I or II
- 6-minute walk distance ≥380 m to 440 m
- Normalization of RV function
- Normalization of biomarkers
- Prevention of hospitalization or clinical deterioration
- Peak oxygen consumption of >15 mL/min/kg

McLaughlin VV, et al. *J Am Coll Cardiol*. 2013;62(25 suppl):D73-D81.

Treatment Failures

Component	Definition
Hospitalization for worsening PAH	Any hospitalization for worsening PAH, lung or heart and lung transplantation, atrial septostomy, or initiation of parenteral prostanoid therapy
Disease progression	A decrease of >15% from baseline in the 6-minute walk distance combined with WHO FC III or IV symptoms
Unsatisfactory long-term clinical response	Any decrease from baseline in 6-minute walk distance and WHO FC III symptoms assessed

Galiè N, et al. *N Engl J Med*. 2015;373:834-844.

Oral Therapies

PDE-5 Inhibitors (PDE-5i)

Endothelin Receptor Antagonists (ERA)

PDE-5 Inhibitors

Medication	Indication	Dosing
Sildenafil	Improves exercise ability in early-stage PAH	20 mg PO TID 10 mg IV TID (short-term use in patients unable to take PO)
Tadalafil	Improves exercise ability	40 mg PO daily – Initiate 20 mg if renal/hepatic impairment or concurrent ritonavir – Avoid if CrCL <30 mL/min

TID = three times daily; PO = by mouth; CrCL = creatinine clearance.
US Food and Drug Administration [website]. Drugs@FDA: FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed February 28, 2018.

Endothelin Receptor Antagonists

Medication	Indication	Dosing	Pharmacologic Properties and Other Special Considerations
Bosentan	Improves exercise ability and decreases rate of clinical worsening in WHO FC III-IV	62.5 mg PO BID, then 125 mg PO BID after 4 weeks	- Dual antagonist of ET-1_A and -1_B receptors - Tracleer® Access Program (REMS: LFTs, Hb, pregnancy at baseline; monthly LFTs and pregnancy tests; every 3 months Hb)
Bosentan (FDA Approval September 2017)	WHO group 1	32-mg tablet for oral suspension	Approved for pediatric patients aged 3 years and older with idiopathic or congenital PAH
Ambrisentan	WHO FC II-III	10 mg PO daily	- Selective ET-1_A antagonist - Letairis® Education and Access Program (REMS: LFTs, Hb, pregnancy at baseline; monthly pregnancy tests)
Macitentan	Delays progression of PAH	10 mg PO daily	- Tissue selective - Lipophilic - Dual antagonist of ET-1_A and -1_B receptors - Opsumit® (REMS: LFTs, Hb, pregnancy at baseline; monthly pregnancy tests)

BID = twice daily; REMS = risk evaluation and mitigation strategy; Hb = hemoglobin; LFTs = liver function tests; Hb = hemoglobin; FDA = US Food and Drug Administration.
US Food and Drug Administration [website]. Drugs@FDA: FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed February 28, 2018.

Macitentan

Primary and Secondary Endpoints for Events Related to PAH and Death

Endpoint	Placebo (N=250)	Macitentan 3 mg (N=250)	Macitentan 10 mg (N=242)	Macitentan 3 mg vs Placebo		Macitentan 10 mg vs Placebo	
	No. of Patients (%)			Hazard Ratio (97.5% CI)	*P* Value	Hazard Ratio (97.5% CI)	*P* Value
Event related to PAH or death as the first event							
All events	116 (46.4)	95 (38.0)	76 (31.4)	0.70 (0.52-0.96)	.01	0.55 (0.32-0.76)	<.001
Worsening of PAH	93 (37.2)	72 (28.8)	59 (24.4)				
Death from any cause	17 (6.8)	21 (8.4)	16 (6.6)				
Prostanoid initiation	6 (2.4)	1 (0.4)	1 (0.4)				
Lung transplantation	0	1 (0.4)	0				
Death due to PAH or hospitalization for PAH as the first event							
All events	84 (33.6)	65 (26.0)	50 (20.7)	0.67 (0.46-0.97)	.01	0.50 (0.34-0.75)	<.001
Hospitalization for PAH	79 (31.6)	56 (22.4)	45 (18.6)				
Death due to PAH	5 (2.0)	9 (3.6)	5 (2.1)				
Death from any cause	19 (7.6)	21 (8.4)	14 (5.8)	0.97 (0.48-1.98)	.92	0.64 (0.29-1.42)	.20
Death due to PAH	14 (5.6)	14 (5.6)	7 (2.9)	0.87 (0.37-2.04)	.72	0.44 (0.16-1.25)	.07
Death from any cause by the end of the study	44 (17.6)	47 (18.8)	35 (14.5)	1.05 (0.65-1.67)	.83	0.77 (0.46-1.28)	.25

Pulido T, et al. *N Engl J Med*. 2013;369:809-818.

Prostacyclins

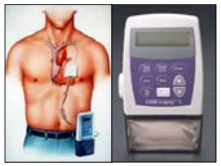
Epoprostenol

Treprostinil

Iloprost

Treprostinil

IV CADD-Legacy® Pump



SQ CADD-MS®3 Pump

Tyvaso® Inhalation System

SQ MiniMed® Pump

Crono® Five pump

US Food and Drug Administration [website]. Medical Devices. https://www.fda.gov/MedicalDevices/default.htm. Accessed February 28, 2018.

Iloprost

I-neb® AAD® System

AAD = adaptive aerosol delivery.
US Food and Drug Administration [website]. Drugs@FDA: FDA Approved Drug Products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&appIno=021779. Accessed February 28, 2018.

Parenteral Prostacyclins

Medication	Indication	Dosing	Pharmacologic Properties and Other Special Considerations
Epoprostenol IV	WHO FC III-IV	2 ng/kg/min titrated to dose-limiting adverse effects (usual range, 20-40 ng/kg/min)	- Half-life 4-6 minutes - Back-up cassette/pump - Protect from light - Ice pack (Flolan® only) - Requires reconstitution and further dilution (0.9% saline or sterile water: Veletri®; special diluent: Flolan®) - Every 24-hour cassette change
Treprostinil SC	WHO FC II-IV	1.25 ng/kg/min titrated to dose-limiting adverse effects (usual range, 40-80 ng/kg/min)	- Half-life 4 hours - Back-up pump - Stable at room temperature - SQ: Undiluted, every 72-hour syringe change - IV: Requires further dilution, every 48-hour cassette change
Treprostinil IV	WHO FC II-IV		

US Food and Drug Administration [website]. Drugs@FDA: FDA Approved Drug Products. https://www.fda.gov/Drugs/default.htm. Accessed February 28, 2018.

Inhaled Prostacyclins

Medication	Indication	Dosing	Other Special Considerations
Iloprost	WHO FC III-IV	2.5-5 mcg given 6-9 times per day (maximum, 45 mcg/d)	- Only administered via I-neb® AAD® System - Use higher concentration ampule (20 mcg/mL) for patients with extended treatment time or at 5-mcg dose
Treprostinil	Increases walk distance in WHO FC III	- 3 breaths QID - Titrate by 3 breaths every 1-2 weeks up to 9 breaths QID	- Only administered via Tyvaso® Inhalation System

QID = four times daily.
US Food and Drug Administration [website]. Drugs@FDA: FDA Approved Drug Products. https://www.fda.gov/Drugs/default.htm. Accessed February 28, 2018.

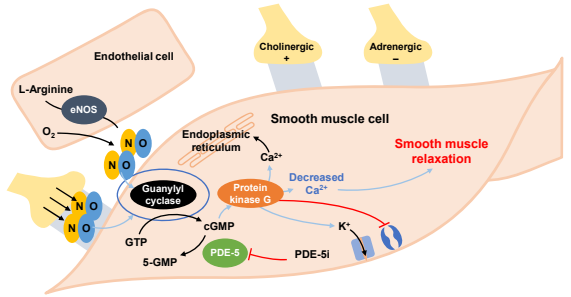
Newer Oral Therapies

Riociguat

Oral Treprostinil

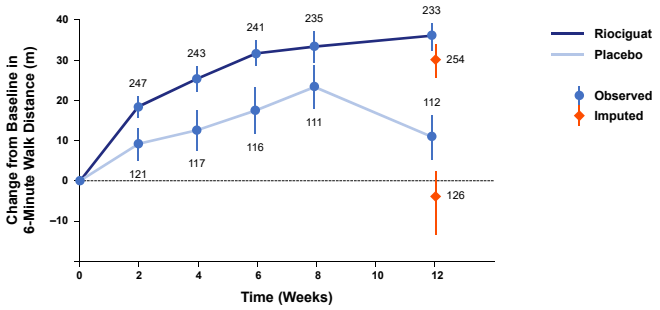
Selexipag

Riociguat



eNOS = endothelial nitric oxide synthase; 5-GMP = guanosine 5′-monophosphate; PDE-5 = phosphodiesterase-5; PDE-5i = phosphodiesterase-5 inhibitor.
US Food and Drug Administration [website]. Drugs@FDA: FDA Approved Drug Products. https://www.fda.gov/Drugs/default.htm. Accessed February 28, 2018.

Riociguat (cont)



Ghofrani H-A, et al. *N Engl J Med*. 2013;369:330-340.

Riociguat (cont)

- Indicated to improve exercise capacity, WHO FC, and delay clinical worsening in patients with:
  - PAH
  - Persistent/recurrent chronic thromboembolic pulmonary hypertension (after surgery or for inoperable disease)
- Initiate 1 mg PO TID; titrate in 0.5-mg increments every 2 weeks up to 2.5 mg PO TID
  - Start 0.5 mg PO TID if risk for hypotension or with concomitant strong CYP and P-gp inhibitors
  - Avoid if CrCL <15 mL/min or if on hemodialysis
- Adempas® REMS program (teratogenicity)

CYP = cytochrome P450; P-gp = p-glycoprotein.
US Food and Drug Administration [website]. Drugs@FDA: FDA Approved Drug Products. https://www.fda.gov/Drugs/default.htm. Accessed February 28, 2018.

Treprostinil Diolamine Extended Release

- Indicated to improve exercise capacity in patients with WHO FC II-III symptoms
- Initiate 0.25 mg PO BID or 0.125 mg PO TID
- Titrate by 0.125- to 0.5-mg PO increments BID to TID every 3 to 4 days or longer
- Maximum dosing per patient tolerability
- Administer with food to improve bioavailability
  - High calorie, high-fat meal

US Food and Drug Administration [website]. Drugs@FDA: FDA Approved Drug Products. https://www.fda.gov/Drugs/default.htm. Accessed February 28, 2018.

Selexipag

- Selective IP-receptor agonist
- Type of prostanoid receptor found in lungs (regulates vascular tone, platelet activity, immunologic responses)
- Similar mode of action to prostacyclin, but a non-prostanoid
- Approved to delay disease progression and reduce risk of hospitalization for patients with PAH
- Initiate 200 mcg PO BID and uptitrate weekly as tolerated to a maximum of 1600 mcg PO BID

US Food and Drug Administration [website]. Drugs@FDA: FDA Approved Drug Products. https://www.fda.gov/Drugs/default.htm. Accessed February 28, 2018.

Selexipag (cont)

Endpoints Related to PAH and Death

Endpoint	Placebo (N=582)	Selexipag (N=574)	Hazard Ratio (99% or 95% CI)	*P* Value
	No. of Patients (%)			
Primary endpoint: Composite of death or a complication related to PAH up to the end of the treatment period				
All events	242 (41.6)	155 (27.0)	0.60 (0.46-0.78)	<.001
Hospitalization for worsening of PAH	109 (18.7)	78 (13.6)		
Disease progression	100 (17.2)	38 (6.6)		
Death from any cause	18 (3.1)	28 (4.9)		
Initiation of parenteral prostanoid therapy or long-term oxygen therapy for worsening of PAH	13 (2.2)	10 (1.7)		
Need for lung transplantation or balloon atrial septostomy for worsening of PAH	2 (0.3)	1 (0.2)		
Secondary endpoint: Death due to PAH or hospitalization for worsening of PAH up to the end of the treatment period				
All events	137 (23.5)	102 (17.8)	0.70 (0.54-0.91)	.003
Hospitalization for worsening of PAH	123 (21.1)	86 (15.0)		
Death due to PAH	14 (2.4)	16 (2.8)		
Secondary endpoint: Death up to the end of the study				
Death due to PAH	83 (14.3)	70 (12.2)	0.86 (0.63-1.18)	.18
Death from any cause	105 (18.0)	100 (17.4)	0.97 (0.74-1.28)	.42

Sitbon O, et al. *N Engl J Med*. 2015;373:2522-2533.

Adverse Reactions

Medication/Class	Reaction
PDE-5i	Headache, dyspepsia, flushing, epistaxis, insomnia, hypotension, visual changes
Riociguat	Headache, dizziness, dyspepsia, gastroesophageal reflux, nausea, diarrhea, vomiting, hypotension, anemia, constipation, teratogenicity
ERAs	Headache, flushing, peripheral edema, nasal congestion, sinusitis, transaminitis, liver injury, anemia, teratogenicity
Prostacyclins	Nausea, vomiting, diarrhea, flushing, jaw pain, headache, rash, erythema, hypotension, leg pain – *Inhaled: Cough, throat irritation*
Selexipag	Headache, diarrhea, jaw pain, nausea, myalgia, vomiting, extremity pain, flushing

ERA = endothelin receptor antagonist.
Galiè N, et al. *Eur Heart J*. 2016;37:67-119.

Parenteral Prostacyclins: Line-Related Complications

- **SQ:** Injection-site pain, swelling
  - Preemptive site management (eg, topical analgesics)
- **IV:** Catheter-related infection, bacteremia, thrombosis
  - ↑ risk of Gram-negative infection (treprostinil > epoprostenol)
- Need for extensive education/training, support

Galiè N, et al. *Eur Heart J*. 2016;37:67-119.

Drug Interactions

Medication/Class	Interaction
PDE-5i	Strong CYP3A4 inhibitors/inducers, nitrates, alpha-blockers, alcohol
Riociguat	Strong CYP and P-gp inhibitors/inducers, PDE-5is, non-specific PDE inhibitors (eg, theophylline, dipyridamole), nitrates, antacids, smoking
ERAs	Strong CYP3A4 and CYP2C19 inhibitors/inducers, warfarin, oral contraceptives – *Bosentan: Cyclosporine, glyburide*
Prostacyclins	Vasodilators, antiplatelets, anticoagulants – *Treprostinil: Gemfibrozil, rifampin*
Selexipag	Strong CYP2C8 inhibitors

CYP = cytochrome P450; P-gp = p-glycoprotein.
Galiè N, et al. *Eur Heart J*. 2016;37:67-119.

Adjunctive Treatments

- Diuretics
- Digoxin
- Oxygen
- Warfarin

Patient Case

- HL is a 43-year-old mother of three who presented with a 2-month history of dyspnea on exertion and fatigue consistent with class II to class III symptoms
- She reports a 1-year use of phentermine for weight loss prior to symptom onset
- She also reports that her mother had PAH and died at the age of 47 years
- She was diagnosed with PAH (heritable vs drug-induced) based on RHC

PAH = pulmonary arterial hypertension; RHC = right heart catheterization.

Patient Case (cont)

Which medication would you recommend for HL?

1. PDE-5i
2. Epoprostenol
3. ERA
4. PDE-5i + ERA
5. Inhaled prostacyclin

Treatment Guidelines

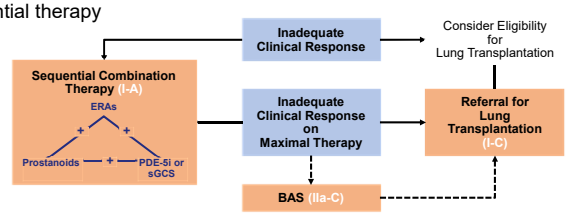
Initial Therapy with PAH-Approved Drugs

Recommendation	Evidence[a]	WHO FC II	WHO FC III	WHO FC IV
I	A or B	Ambrisentan Bosentan Macitentan[b,c] Riociguat[b] Sildenafil Tadalafil	Ambrisentan Bosentan Epoprostenol IV Iloprost inhaled Macitentan[b,c] Riociguat[b] Sildenafil Tadalafil Treprostinil SC inhaled[b]	Epoprostenol IV
IIa	C		Iloprost IV[b] Treprostinil IV	Ambrisentan Bosentan Iloprost inhaled and IV[b] Macitentan[b,c] Riociguat[b] Sildenafil Tadalafil Treprostinil SC, IV, inhaled[b]
IIb	B		Beraprost[b]	
	C		Initial Combination Therapy	Initial Combination Therapy

Orange: Morbidity and mortality as primary endpoint in randomized controlled study or reduction in all-cause mortality (prospectively defined). [a]Level of evidence is based on the WHO-FC of the majority of the patients of the studies. [b]Approved only: By the FDA (macitentan, riociguat, treprostinil inhaled); in New Zealand (iloprost IV); in Japan and S. Korea (beraprost). [c]Positive opinion for approval of the CHMP of EMA.
Galiè N, et al. *J Am Coll Cardiol*. 2013;62:D60-D72.

Approaches to the Treatment of PAH

- Sequential therapy



- Up-front combination therapy
  - AMBITION trial (tadalafil + ambrisentan vs monotherapy with either)
  - Hazard ratio, 0.50 (95% CI, 0.35-0.72; *P*<.001) for composite of clinical failure events in favor of combination group vs pooled monotherapy

sGCS = soluble guanylate cyclast stimulator; BAS = balloon atrial septostomy.
Galiè N, et al. *J Am Coll Cardiol.* 2013;62(25 suppl): D60-D72.

Specialty Pharmacy

- Complex and costly medications/delivery systems
- Types of services
  - Clinical counseling and support
  - Local nursing support and training
  - Prior authorization
  - Medication delivery

Kaae S, et al. *Res Soc Admin Pharm*. 2012;8(3):253-257. ReCept pharmacy [website]. http://receptrx.com/prescriber/. Accessed April 18, 2018.

Medication Safety

- Ensure communication across transitions of care
- Policy/protocol/guideline development and oversight
- Prostacyclin vigilance
  - Determine essential order details for prostacyclins: type of agent, route, pump, timing of next dose, dosing weight, current dose, titration schedule, vial concentration (treprostinil) or vial size (epoprostenol), amount of medication and diluent for mixing, type of diluent, infusion rate, back-up cassette availability (epoprostenol)

Coons JC, et al. *Am J Health-Syst Pharm*. 2013;70:1716-1723.

Patient Counseling

- Expectations from treatment/goals of care
- Dosing/administration/product preparation
- Catheter and line care
- Adherence
- Specialty pharmacy and nursing contact
- Maintaining accurate medication list
- Updated dosing sheet from specialty pharmacy
- Monitoring and follow-up
- Symptom recognition
- Emotional support
- Adverse events
- Health maintenance
  - Diet/exercise
  - Immunizations
  - Pregnancy/contraception

Poms A, et al. Support care for the pulmonary hypertension patient. In: Maron B, et al (eds). *Pulmonary Hypertension*. Cham, Switzerland: Springer; 2016.

PAH "Clinical Pearls"

- Improved clinical outcomes have been realized in PAH through advancements in pharmacotherapy
- There are now 14 FDA-approved medication formulations with more in the pipeline
- Pharmacists are well-positioned, and essential, to safe and effective PAH care in a team-based setting

Questions?

Thank you for your attention!