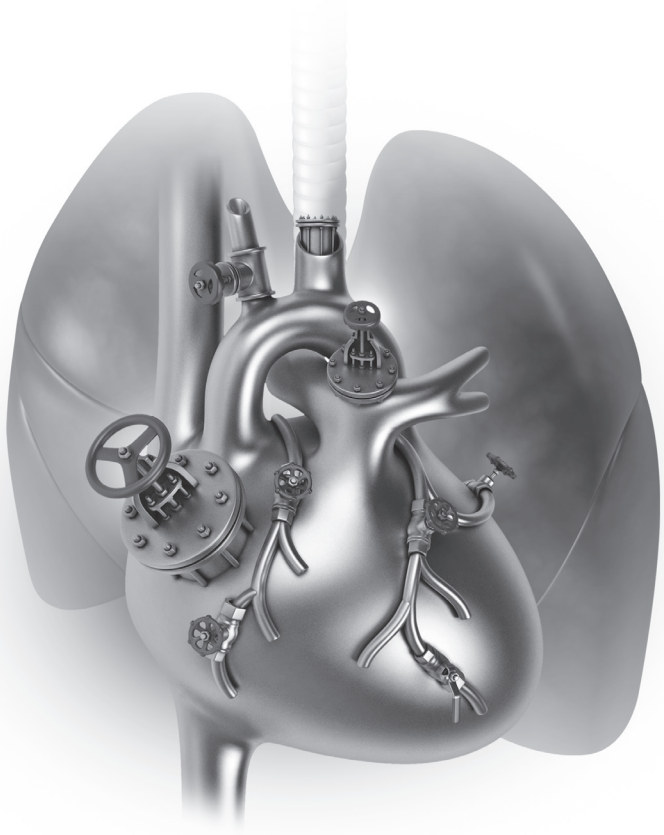


EDUCATIONAL PROGRAM

Overview

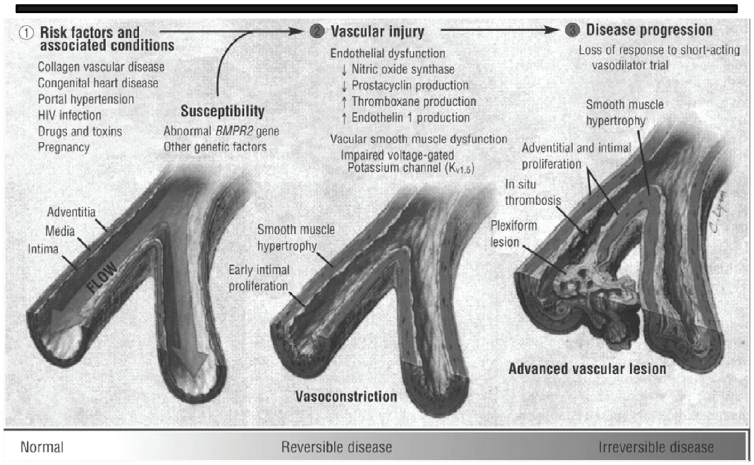
- Diagnosis and classification of pulmonary hypertension
- Etiology and pathophysiology of pulmonary hypertension
- Introduction and pharmacology of currently approved therapies
- Clinical use of currently approved treatments and evidence for use within each classification of pulmonary hypertension
- Interactive case: PH vs. PAH:
  - Two cases that present similarly but result in two very different therapy and management plans

Pulmonary Hypertension (PH)

- Broadly defined as mean pulmonary artery pressure (mPAP) ≥ 25 mmHg
- Sustained PH can lead to right heart failure
  - Pulmonary vasculature normally a low pressure circuit
  - Increased pulmonary artery pressure increases pulmonary vascular resistance (PVR) and increases workload on right heart
    - Right heart not as adaptable to high pressure
- Associated with 1-year mortality up to 10-15%

Benza, et al. *Chest* 142(2), 448-456 (2012).
Thenappan, et al. *Eur. Respir. J.* 30(6), 1103–1110 (2007).

PH Progression



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

Diagnosis of PH

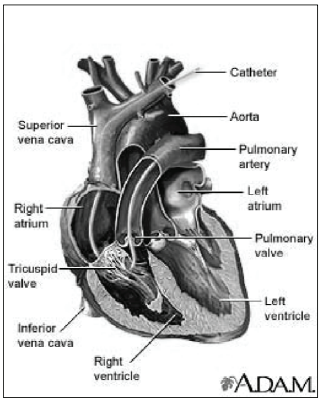
- Because of non-specific signs and symptoms, often diagnosed late in disease progression

Common Initial Symptoms (N=187)	Patients (%)
Dyspnea	60
Fatigue	19
Syncope or near syncope	13
Chest pain	7
Palpitations	5
Leg edema	3

McGoon et al. *Chest.* 126:14S-34S (2004).
Rich S et al. *Ann Intern Med.* 107:216-223 (1987).

Diagnosis of PH

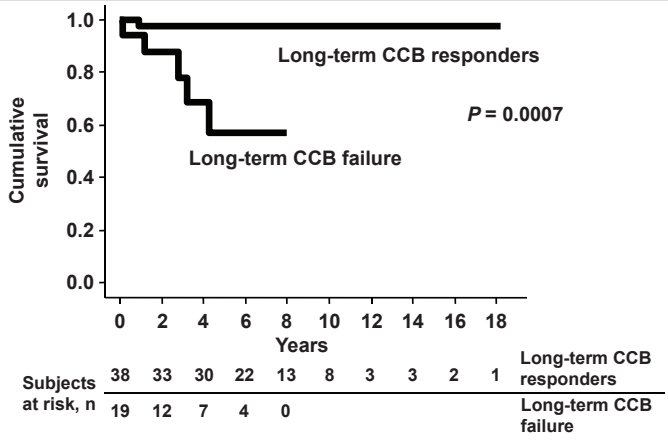
- Pulmonary artery pressure can be estimated on echocardiogram
  - Using tricuspid regurgitation
- PH must be confirmed by right heart catheterization
  - PAP and pulmonary capillary wedge pressure (PCWP) are measured before and after vasodilator challenge
  - Along with echo, provides data needed to classify type of PH
    - Category of PH crucial to developing effective treatment plan



Acute Vasodilator Responders

- Definition of vasodilation response:
  - Fall in mPAP ≥ 10 mm Hg
  - mPAP (absolute) < 40 mm Hg
  - Normal CO (4-6 L/min)
- Only a small subset of PAH patients meet response definition (<10%)
- Responders are good candidates for calcium channel blocker (CCB) trial
  - Long-term CCB responders (50% of vasodilator responders) experience significant reductions in mortality

CCB Response and Mortality

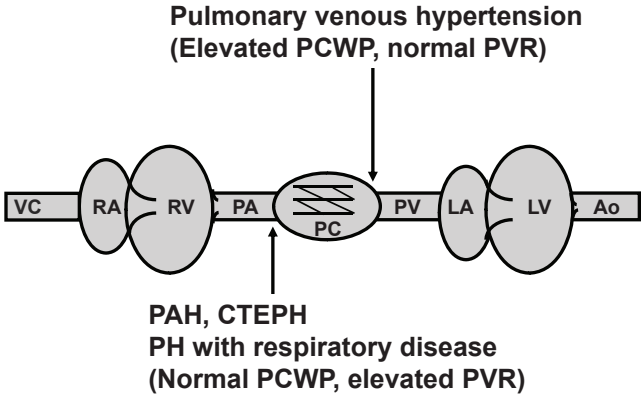


Sitbon, et al. *Circulation.* 111:3105-3111 (2005).

PH Classification

- Classified by WHO into 5 broad categories, each with different etiology:
  - Group 1: Pulmonary arterial hypertension
  - Group 2: PH due to left heart disease
  - Group 3: PH due to lung disease and/or hypoxia
  - Group 4: Chronic thromboembolic PH
  - Group 5: PH with unclear multifactorial mechanisms

Hemodynamic Differences in PH



Group 1: Pulmonary Arterial Hypertension (PAH)

- Most well-known and well-studied type of PH
  - Actually a rare disease (15-26 cases/million)
- Involves components of vasoconstriction, proliferation, and inflammation
  - Imbalance of vasodilators (NO) and vasoconstrictors (ET-1) in pulmonary vasculature
  - Proliferation and inflammation lead to vascular fibrosis and narrowing of pulmonary arteries
- Tends to occur more commonly in women
- PAH can also be heritable
  - 80% from mutations in bone morphogenic protein receptor 2 (BMPR2)

Humbert, et al. *Am. J. Respir. Crit. Care Med.* 173(9), 1023–1030 (2006).
Peacock, et al. *Eur. Respir. J.* 30(1), 104–109 (2007).
Machado, et al. *Hum. Mutat.* 27(2), 121–132 (2006).

Group 2: PH Due to Left Heart Disease

- Associated with pulmonary venous hypertension, which often leads to pulmonary arterial hypertension
  - mPAP ≥ 25mmHg and PCWP ≥ 15 mmHg
  - Most often from valvular disease or left heart failure
    - Estimated that 30-40% of heart failure patients have disproportionately high mPAP compared to degree of heart failure
    - Elevated mPAP in HF patients are associated with increased risk of death

Lam, et al. *J. Am. Coll. Cardiol.* 53(13), 1119–1126 (2009).
Schwartzenberg, et al, *J. Am. Coll. Cardiol.* 59(5), 442–451 (2012).
Bursi, et al. *J. Am. Coll. Cardiol.* 59(3), 222–231 (2012).

Group 3: PH Due to Lung Disease and/or Hypoxia

- Associated with hypoxic lung disease, often COPD or interstitial lung disease (ILD)
  - Thought to be common in advanced stage lung disease
  - Actual prevalence not well-defined
- Out-of-proportion PH is associated with 50% or greater increase in mortality
- No large RCTs exist addressing long term effects of PH treatments in this patient population

Oswald-Mammosser, et al. *Chest* 107(5), 1193–1198 (1995).
Lettieri et al. *Chest* 129(3), 746–752 (2006).
Hoeper, et. al. *J. Am. Coll. Cardiol.* 54(Suppl. 1), S85–S96 (2009).

Group 4: Chronic Thromboembolic PH

- Defined as mPAP ≥25 mmHg persisting longer than 6 months after diagnosis of pulmonary embolism
  - Found in approximately 4% of PE patients
- Can be curable by pulmonary thromboendarectomy
- If inoperable, vasodilators, such as riociguat, may be beneficial

Condliffe, et al. *Am. J. Respir. Crit. Care Med.* 177(10), 1122–1127 (2008).

Group 5: PH with Unclear Multifactorial Mechanisms

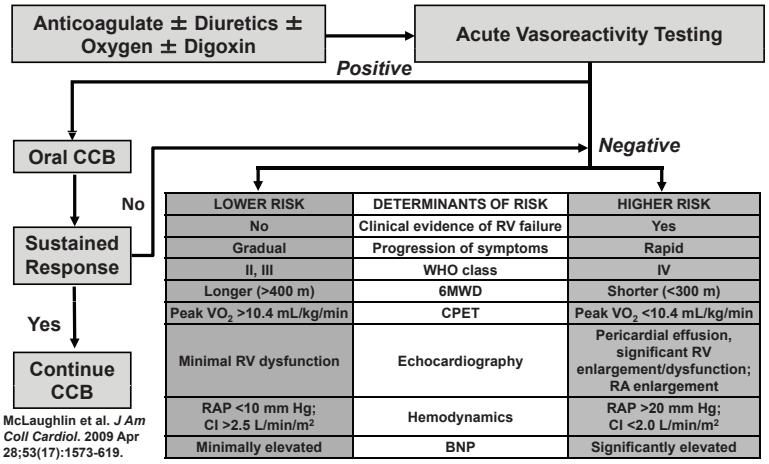
- Multiple miscellaneous etiologies, most of which are not well-studied.
  - Most common etiology in the North America is thought to be sarcoidosis
    - PH is estimated to be present in nearly ¾ of patients with advanced sarcoidosis
    - Etiology not well understood, but may involve pulmonary fibrosis or formation of vascular flow-inhibiting granulomas
- Few treatment studies have been done in these patient populations

Shigemitsu et al. *Curr. Opin. Pulm. Med.* 13(5), 434–438 (2007).
Baughman et al. *Am. J. Respir. Crit. Care Med.* 183(5),573–581 (2011).

Goals of Treatment in PH

- Improvement in the patient's symptoms, quality of life, and survival.
  - Includes slowing the progression or preventing right heart failure.
- Objective measurements of treatment response include
  - Improvement in WHO Functional Class
    - Mirror New York Heart Association functional classes in heart failure
  - Exercise capacity
    - 6-min walk distance (6MWD)
    - Cardiopulmonary exercise test
    - Treadmill test
  - Hemodynamics obtained from RHC
  - Survival

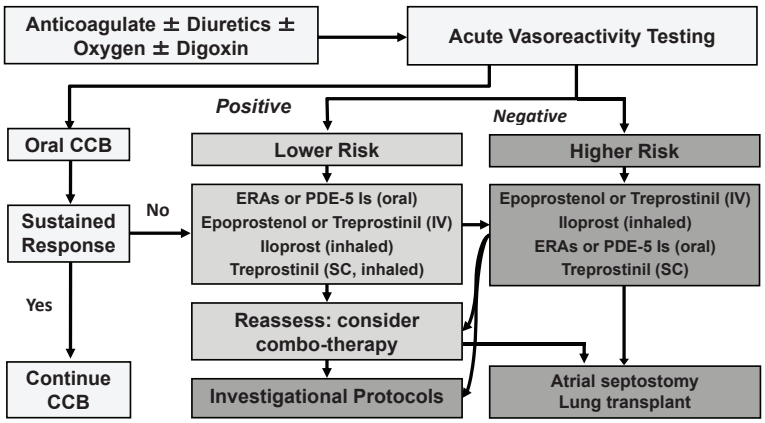
What is the Optimal Treatment Strategy?



LOWER RISK	DETERMINANTS OF RISK	HIGHER RISK
No	Clinical evidence of RV failure	Yes
Gradual	Progression of symptoms	Rapid
II, III	WHO class	IV
Longer (>400 m)	6MWD	Shorter (<300 m)
Peak VO_2 >10.4 mL/kg/min	CPET	Peak VO_2 <10.4 mL/kg/min
Minimal RV dysfunction	Echocardiography	Pericardial effusion, significant RV enlargement/dysfunction; RA enlargement
RAP <10 mm Hg; CI >2.5 L/min/m^2	Hemodynamics	RAP >20 mm Hg; CI <2.0 L/min/m^2
Minimally elevated	BNP	Significantly elevated

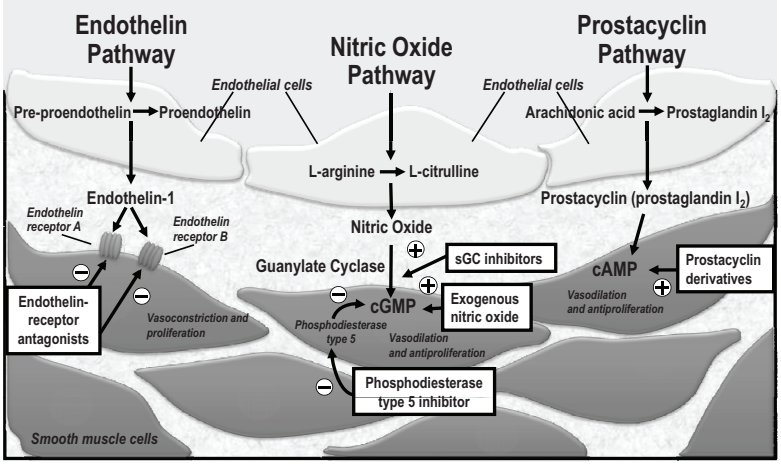
McLaughlin et al. *J Am Coll Cardiol*. 2009 Apr 28;53(17):1573-619.

ACCF/AHA Consensus PAH Treatment Algorithm



McLaughlin et al. *J Am Coll Cardiol*. 2009 Apr 28;53(17):1573-619.

Therapeutic Targets for PAH



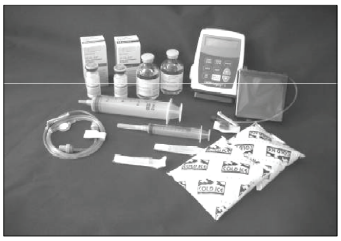
Humbert et al. *N Engl J Med*. 351:1425-1436 (2004).

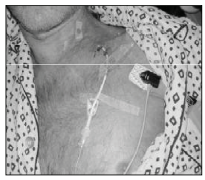
Prostacyclin Analogues: Overview

- Prostacyclin pathway: prostacyclin is a naturally occurring vasodilator
  - Activates process that promotes vasodilatory, anti-platelet, and anti-proliferative effects
- Differ in stability, half-life, and method of delivery
- Available only through restricted drug distribution system (RDDS)
- Typically initiated with close supervision in clinical setting, infusions titrated to response and tolerability
- Require extensive patient education and training
- Interruptions must be avoided

Epoprostenol Sodium

How Supplied	Administration	FC	Dose	Properties	CI/P	Misc.
Generic Flolan® Veletri*® 0.5mg, 1.5mg *RTS formulation with expanded stability	**Continuous IV infusion via infusion pump. Requires tunneled CVC. Flolan requires use of ice packs. Requires reconstitution.**	**III, IV**	**Initiated at 2 ng/kg/min and titrated based on response. Ongoing: 1-2 ng/kg/min q1-2wk.**	**$T_{½}$ <6 min. Temp and light sensitive. Reconstituted stability dependent on formulation. Rapidly hydrolyzed in the blood.**	**CHF due to severe LVD. Avoid abrupt withdrawals or interruption in infusion: may result in rebound PH or death.**	**Initiated in controlled setting. Monitor for signs of BSI.**

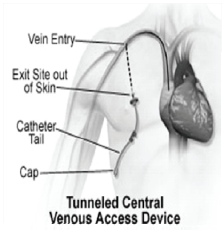




Treprostinil Sodium

How Supplied	Administration	FC	Dose	Properties	CI/P	Misc.
Remodulin® 1mg/mL, 2mg/mL, 5mg/mL, 10mg/mL in 20mL vials **Tyvaso® for inhalation 0.6 mg/mL in 2.9mL ampules** *Orenitram® 0.125mg, 0.25mg, 1mg and 2.5mg ER tablets**	**Continuous IV or SubQ infusion via infusion pump. IV requires tunneled CVC. Intermittent inhalation via dedicated inhalation device.** ***FDA Approved oral formulation on 12/20/2013. Launch date TBD.***	**Infused: II-IV Inhaled: primarily III**	**Initiated at 1.25 ng/kg/min and titrated based on response Ongoing: 1.25 ng/kg/min every week or as tolerated** **Inhaled: start at 3 breaths QID, titrated to goal 9 breaths QID.**	**$T_{½}$ ~4 hours. Metabolized by CYP 2C8. Diluted: 48 hour infusion duration. Undiluted: 72 hour infusion duration. Inhaled: protect ampules from light during storage. Once opened: discard remaining solution after 24 hours**	**CHF due to severe LVD. Avoid abrupt withdrawals or interruption in infusion: may result in rebound PH or death.**	**Initiated in controlled setting such as a hospital Monitor for signs of BSI One inhaled ampule provides multiple doses/day**

Treprostinil Administration

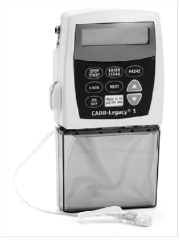


Tunneled Central Venous Access Device

Breaths/session

microL/hr

mL/hr



mL/24 hr

Iloprost Sodium						
How Supplied	Administration	FC	Dose	Properties	CI/P	Misc.
Ventavis® 10 mcg/mL and 20 mcg/mL unit dose ampules	Intermittent inhalation via dedicated inhalation device	III, IV	Initial: 2.5mcg x once, then 5mcg per dose if tolerated for 6 to 9 treatments/ day.	$T_{½}$ ~20 to 30 min. Store at RT Discard unused solution	Caution if underlying lung disease or symptomatic hypotension. Bronchospasm	One ampule used per treatment session (20mcg/mL = 5mcg dose only!)

Ampule Concentration	Dose	Chamber/Disc Color
10 mcg/mL	2.5 mcg	Red
10 mcg/mL	5 mcg	Purple
20 mcg/mL	5 mcg	Gold

Prostacyclin Adverse Effects

- **General side effects**
  - Jaw pain
  - Flushing
  - Diarrhea
  - Headache
  - Nausea/vomiting
  - Leg pain
  - Rash
  - Reduced platelets
- **Subcutaneous**
  - Site pain/irritation
  - Site infection
- **Intravenous**
  - Thrombus formation
  - CVC infection
  - Sepsis
- **Inhaled**
  - Cough
  - Throat irritation/pain

Endothelin Receptor Antagonists: Overview

- Endothelin pathway: endothelin binds to ET_A and ET_B receptors → regulation of vascular tone
  - ET_A activation = vasoconstriction and cellular proliferation
- ERAs antagonize ET_A receptors*
- Available only through restricted drug distribution system (RDDS)
- Risk Evaluation and Mitigation Strategies (REMS)
- Oral formulation

* bosentan and macitentan are dual ET_A and ET_B receptor antagonists.

Bosentan				
How Supplied	**REMS**		**Properties**	**CI/P**
Tracleer® 62.5mg, 125mg tablets	Teratogenicity, liver toxicity. Must enroll in Tracleer Access Program (TAP).		$T_{½}$ ~5 hours Metabolized and strong inducer of CYP3A4 and CYP2C9, possibly CYP2C19; Caution with drug intx.	CI: Pregnancy and use of cyclosporine or glyburide. Caution with liver disease.
	FC	**Dose**		
Administration	II-IV	Initial: 62.5mg BID x 4 weeks, then increase to 125mg BID thereafter if tolerated and wt >40kg.		
Oral tablets. Can be dissolved into soln.				

Ambrisentan				
How Supplied	**REMS**		**Properties**	**CI/P**
Letairis® 5mg, 10mg tablets	Teratogenicity. FRP must enroll in Letairis Education and Access Program (LEAP).		$T_{½}$ up to ~15 hours Metabolized by CYP3A4 and CYP2C19, substrate of P-glyco-protien	CI: pregnancy and IPF. Caution with anemia, fluid retention, PVOD.
	FC	**Dose**		
Administration	II-III	Initial: 5mg daily, increase to 10mg daily if tolerated		
Oral tablets				

Macitentan				
How Supplied	**REMS**		**Properties**	**CI/P**
Opsumit® 10mg tablets	Teratogenicity. FRP must enroll in Opsumit REMS Program		$T_{½}$ ~ 16 hrs (48 hrs for active metabolite) Metabolized by CYP3A4 and CYP2C19; active metabolite contributes ~ 40% of activity.	CI: Pregnancy Caution with anemia, liver disease.
	FC	**Dose**		
Administration	Mostly II-III	10mg po daily		
Oral tablets				

SERAPHIN Trial Primary Endpoint

Clinical Event

- Death
- Atrial Septostomy
- Lung transplant
- PGI2 infusion initiation
- Worsening of PAH
  - Reduced 6 MWD
  - Worsening FC
  - New drug added

Pulido T, et al. *N Engl J Med* 2013;369:809-18.

ERA Adverse Effects

Common

- Headache
- Flushing
- Peripheral edema
- Nasal congestion
- Sinusitis
- Elevated LFT's

Serious

- Anemia
- CHF exacerbation
- Liver injury*
- Birth defects

*Bosentan requires LFT monitoring

PDE-5 Inhibitor Overview

- Nitric oxide (NO) pathway: Release of NO → increased intracellular cGMP → vasodilation
  - PDE-5, predominant PDE in pulmonary vasculature, responsible for degradation of cGMP
- PDE-5 inhibitors increase concentrations of cGMP resulting in vasodilation
- Oral formulation
- Sildenafil available as injectable

Sildenafil

How Supplied	REMS		Properties	CI/P
generic Revatio® 20mg tablets Revatio® 10mg/12.5 mL soln for injection	n/a		$T_{½}$ ~4 hours Metabolized by CYP3A4 and CYP2C9 (minor)	CI: use with organic nitrates. Increased mortality risk in peds. Caution with SCD, PVOD. Post marketing AE: NAION
	FC	Dose		
Administration	Mostly II-III	Oral: 20mg TID Inj.: 10mg TID		
Oral tablets. Can be extemporaneously compounded. Solution for injection used for NPO.				

Tadalafil

How Supplied	REMS		Properties	CI/P
Adcirca® 20mg tablets	n/a		$T_{½}$ ~35 hrs Metabolized by CYP3A4	CI: use with organic nitrates Caution with SCD, PVOD.
	FC	Dose		
Administration	II-III	40mg daily		
Oral tablets				

PDE-5 Inhibitor Adverse Effects

Common

- Headache
- Flushing
- Nausea
- Dyspepsia
- Nasal congestion
- Myalgia (tadalafil)
- Epistaxis (sildenafil)

Serious

- Hypotension
- Vision loss
- Hearing loss
- Priapism
- Vaso-occlusive crisis (sildenafil)
- Mortality with pediatric use (sildenafil)

Guanylate Cyclase Stimulator

- Novel mechanism
- First non-WHO Group 1 approved indication
- Nitric oxide (NO) pathway: NO → guaylate cyclase → inc cGMP → vasodilation
  - Riociguat: soluble guanylate cyclase stimulator (sGC); works both independently of NO or to augment endogenous NO.
- Available only through RDDS
- Risk Evaluation and Mitigation Strategies (REMS)
- Oral formulation

Riociguat				
How Supplied	**REMS**		**Properties**	**CI/P**
Adempas® 0.5mg, 1mg, 1.5mg, 2 mg, 2.5mg tablets	**Teratogenicity, FRP enroll in Adempas REMS program**		**T ½ ~ 12hrs in PAH pts. Substrate of P-gp and BCRP, metabolized by CYP-1A1, 3A, 2C8, 2J2.**	**CI: Pregnancy, nitrates, PDE-5i. Caution with hypotension, PVOD, bleeding, smokers.**
	FC	**Dose**		
Administration	**II-III**	**0.5 to 1mg TID, titrated q2weeks to max 2.5mg TID**		
Oral tablets				

- **Novel mechanism and first targeted therapy approved for a non-WHO Group 1 indication (approved for WHO Group 1 PAH and WHO Group 4 CTEPH)**
- **Must be re-titrated if doses are interrupted for 3 or more days**
- **Smokers may require higher doses**

sGC Adverse Effects

Common

- Headache
- Dizziness
- Dyspepsia
- Nausea
- Diarrhea
- Vomiting
- Constipation
- Peripheral edema

Serious

- Hypotension
- Hemorrhagic events
- Anemia
- Birth defects

WHO Group 2 Pulmonary Hypertension

Drug Class	Strength of Evidence [1]: Treatment Effects of PAH Targeted Therapies
Prostacyclin Analogues	Harmful (moderate)
Endothelin Receptor Antagonists	Harmful (weak)
Phosphodiesterase Inhibitors	Beneficial (weak)
Soluble Guanylate Cyclase Agonist	Neutral (weak)

[1] Strong: supported by multiple randomized clinical trials; moderate: supported by one clinical trial or multiple trials conflict; weak: only small or non-randomized trials available; unknown: not enough data to determine benefit

Duarte J, et al. *Future Cardiol.* 2013 May;9(3):335-49.
Bonderman D, et al. *Circulation*. 2013;128:502-511.

WHO Group 3 Pulmonary Hypertension

Drug Class	Strength of Evidence [1]: Treatment Effects of PAH Targeted Therapies
Prostacyclin Analogues	Neutral (weak)
Endothelin Receptor Antagonists	Neutral (weak)
Phosphodiesterase Inhibitors	Harmful (weak)
Soluble Guanylate Cyclase Agonist	Unknown

[1] Strong: supported by multiple randomized clinical trials; moderate: supported by one clinical trial or multiple trials conflict; weak: only small or non-randomized trials available; unknown: not enough data to determine benefit

Duarte J, et al. *Future Cardiol.* 2013 May;9(3):335-49.

WHO Group 4 Pulmonary Hypertension

Drug Class	Strength of Evidence [1]: Treatment Effects of PAH Targeted Therapies
Prostacyclin Analogues	Beneficial (weak)
Endothelin Receptor Antagonists	Neutral (moderate)
Phosphodiesterase Inhibitors	Beneficial (weak)
Soluble Guanylate Cyclase Agonist	Beneficial (strong)

[1] Strong: supported by multiple randomized clinical trials; moderate: supported by one clinical trial or multiple trials conflict; weak: only small or non-randomized trials available; unknown: not enough data to determine benefit

Duarte J, et al. *Future Cardiol.* 2013 May;9(3):335-49.
Ghofrani H, et al. *N Engl J Med.* 2013;369:319-29.

WHO Group 5 Pulmonary Hypertension

Drug Class	Strength of Evidence [1]: Treatment Effects of PAH Targeted Therapies
Prostacyclin Analogues	Unknown
Endothelin Receptor Antagonists	Unknown
Phosphodiesterase Inhibitors	Unknown
Soluble Guanylate Cyclase Agonist	Unknown

[1] Strong: supported by multiple randomized clinical trials; moderate: supported by one clinical trial or multiple trials conflict; weak: only small or non-randomized trials available; unknown: not enough data to determine benefit

Duarte J, et al. *Future Cardiol.* 2013 May;9(3):335-49.

Challenges with PAH Treatments

- Identifying the pharmacist's role in PAH management
- Transitions in care
- Complexity of regimen
- Infusion-related safety requirements
- Availability of medications and administration devices
- Education and training needs
- Reimbursement

Complex Regimens

- **Dosing and administration**
  - Route
  - Vial concentration
  - Calculated dose
  - Concentration and total volume
  - Device specific infusion rate
  - **Dosing weigh**t
  - Titration orders
  - Timing of next reservoir change

Prostacyclin Infusion-Related Safety Considerations

- ***Contact patients PH specialist***
- Drug interactions and drug stability
- Never stop or turn off pump
- Never flush or prime the line
- No blood draws from dedicated line: consider labeling catheter and tubing
- Line dislodgement or obstruction ➔ place peripheral line temporarily
- Do not infuse with other medications
- "Dead-space" and priming needs
- Need for MRI or X-ray managing pumps
- Backup pump, drug, supplies, mixed cassette
- Home vs. hospital pump
- Suspected infection

….and more…….

Transitioning Therapy

Rationale

Recurrent bacteremia
Clinical Deterioration
Profound improvement (benefits vs. risks)

Intolerable side effects
Limitations with therapy management
Lifestyle, patient preference

Potential concerns

- **Intermittent vs. continuous dosing of prostacyclin**
- **Dose limitations with inhaled therapy**
- **Patient compliance**
- **Follow up**
- **Patient selection**

Types

- **Transitioning parenteral prostacyclins**
  - **Titration**
  - **Rapid**
- **Transitioning inhaled prostacyclins**
- **Parenteral to or from inhaled prostacyclin**
- **Prostacyclin to oral**

Cases of Suspected PH

	Patient 1 Ms H	Patient 2 Ms A
HPI	51 yo AAF for evaluation of PH. Admitted recently for SOB and chest tightness	55 yo AAF for evaluation of PH. Referred from rheum for worsening SOB.
PMH	HTN, OSA, SLE, A-fib	COPD, OSA, DVT/PE, Hep C, DM, SLE, hiatal hernia, diverticulitis, fibromyalgia
SH/FH/ Allergies	Tob 1 ppw (used to be 1ppd) for 20yrs social etoh (3-4 beers once a weekend). denies illicits NKDA FH negative	Tob 2 ppd x 35 yrs, quit Negative etoh Previous marijuana use NKDA FH: VTE

Cases of Suspected PH *con't*

	Patient 1 Ms H	Patient 2 Ms A
Meds	potassium daily (unknown dose) aspirin 81mg daily atorvastatin 20mg daily warfarin 7.5mg daily- trazadone qhs (unknown dose) furosemide BID (unknown dose) mag oxide 500mg daily lisinopril daily (unknown dose) fluticasone 2 sp each nostril daily escitalopram 20mg daily	Singulair 10 mg daily, Advair 250/50 mg twice a day, albuterol as needed, lansoprazole 30 mg twice daily, Spiriva 1puff daily , warfarin 5mg daily, prednisone 5 mg daily, simvastatin 20mg daily, amitriptyline 50mg daily, bupropion 150mg daily, calcium carbonate 3 times a day, cyclobenzaprine 10 mg daily dicyclomine 20 mg tid, vitamin D 50,000 units once weekly, gabapentin 300 mg tid insulin glargine 14 units subcutaneously once daily, Plaquenil 400mg daily.
Lab/vitals	BP 120/60 mmHg, HR 67 bpm BNP: 431 cardiac biomarkers negative x 2 TSH, T4 normal Hep B surf ag and Hep C ab negative HIV panel negative ANA detected Titer 1:1280	BP 100/64 mmHg, HR 95 bpm BNP: 4 TSH, T4 normal C3 elevated Hep B surf ag and Hep C ab positive ANA not detected

Cases of Suspected PH *con't*

	Patient 1 Ms H	Patient 2 Ms A
Diagnostic exams	ECHO: severely enlarged RV. RV pressure overload. Reduced RV systolic fx. EF ~ 55 to 60%. Moderately elevated PASP. Normal LFfx. RHC mPAP 56 mmHg, mPCWP 11mmHg LVEDP 12 mmHg, RAP 18 mmHg, RVP 20 mmHg. CO 4.84 (thermal) 4.75 (fick) PVR 8.3 wood units. Negative Vasodilator challenge. Negative V/Q scan PFT's: Low FEV1 and FVC, ratio nl. DLCO 15% pred.	ECHO: RV fx normal. PASP not assessed. Impaired LV relaxation. c/w DD. EF ~ 55 to 60% RHC mPAP 27 mmHg, mPCWP 12 mmHg, LVEDP 19 mmHg, RAP 11 mmHg, RVP 13 mmHg. CO 4.7 (fick) CI 2.5. PVR 3.2 wood units. Negative vasodilator challenge. Negative V/Q scan, evidence of previous PE PFT's: Low FEV1, normal FVC, reduced ratio. DLCO 37% pred.

Cases of Suspected PH *con't*

	Patient 1 Ms H	Patient 2 Ms A
Medication plan	Started on tadalafil 40mg po daily.	Maximize fluid status and blood pressure control. Compliance with CPAP.
Follow-up	Tadalafil cont x 6 months. Symptoms continued to worsen and started on inhaled treprostinil combination tx. Inhaled treprostinil titrated to 9 breaths QID, cont x 2 months Recent admission 12/21 to 12/23 for worsening DOE Repeat RHC and ECHO little improvement PH specialist requests transition from Inhaled to SQ infused prostacyclin	Pt followed regularly by PH specialist every 3 to 6 months. At recent 6 month f/u appt reported no worsening in symptoms and continues to be compliant with CPAP and medications. BP controlled and working on losing weight.

Cases of Suspected PH *con't*

	Patient 1 Ms H
Plan for transition	Clinical evaluation Education and training Referral coordination with specialty pharmacy Planned initiation of therapy Discharge home and plan for follow up Inpatient transition orders: Initiate infusion at 2 ng/kg/min, increase by 2 ng/kg/min daily x 4 days while simultaneously reducing dose of inhaled treprostinil by 25% daily then d/c. Discharge to home on 8 ng/kg/min. Ongoing titrations: increase by 2 ng/kg/min every 3 days to a goal dose of 20 ng/kg/min. Then follow up with MD.

Subcutaneous treprostinil dose guide
CADD MS3 Infusion Pump (3 ml medication reservoir)

Name:	**Ms H**	**Titration Orders**	
Date of Birth:	**51 yo**	**Start Date:**	**1/15/2014**
MRN:	**1111111111**	**Increment:**	**0.004 ml/hr**
Dosing Weight (kg):	**81.7 kg**	**Interval:**	**1 days**
Cartridge Change (hrs):	**72**	**Number of Titrations:**	**20**
Vial Concentration:	**2.5 mg/ml 20ml MDV**		
Initiation Dose:	**2.0 ng/kg/min**		
Initiation Rate:	**0.004 ml/hr**		

Inpatient Titration Plan

Date	Dose (ng/kg/min)	Infusion Rate (ml/hr)	Notes
01/15/14	**2**	**0.004**	**9 breaths QID**
01/16/14	**4**	**0.008**	**6 breaths QID**
01/17/14	**6**	**0.012**	**3 breaths QID**
01/18/14	**8**	**0.016**	**stop inhaled**