

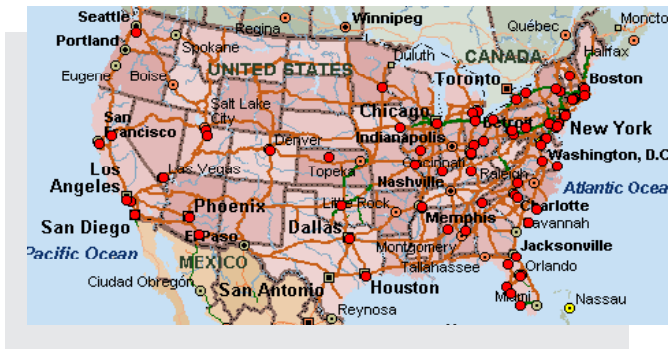
In 2004, the ACCP 1st published guidelines for diagnosing pulmonary arterial hypertension (PAH) in CHEST, the official publication of the American College of Chest Physicians, under the title: "Screening, Early Detection and Diagnosis of Pulmonary Arterial Hypertension: ACCP Evidence Based Clinical Practice Guidelines" (Chest 2004; 126, 14-34)

In order to determine adherence to clinical practice guidelines, a quality enhancement research initiative known as **PAH QuERI** was created. This initiative is supported by a research grant from Actelion Pharmaceuticals to The Canadian Heart Research Centre, a non-for-profit academic research organization of Toronto, Canada.

Participating physicians were provided with guidelines on diagnosis and management of PAH and they were asked to:

- enroll known or newly diagnosed PAH patients into the PAH QuERI database
- use electronic case report forms (eCRFs) at baseline and regular intervals up to 3 years to report patient diagnostic work up, patient management and patient outcomes

### PAH QuERI Study Statistics - site locations



- 61** : Initial number of participating sites
- 57** : Current number of active sites
- 807** : Total patients enrolled

### PAH QuERI Study Progress

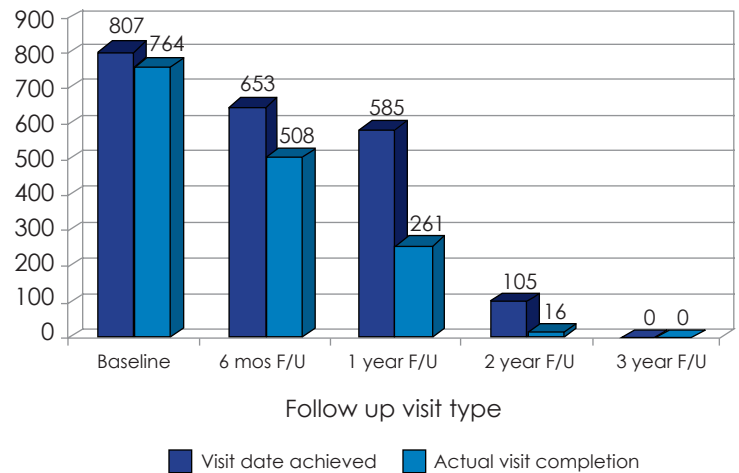
FIRST PATIENT, FIRST VISIT: 16 August, 2005  
 FIRST PATIENT, LAST VISIT: 16 Nov, 2008  
 LAST PATIENT, FIRST VISIT: 05 July, 2007  
 LAST PATIENT, LAST VISIT: 05 October, 2010

Out of 807 patients enrolled, 97% completed baseline, 79% completed the 6 months follow up visit, 70% completed the 1 year follow up visit and 38% completed the 2 year follow up visit

(% completion as of 07 Jan, 2009)

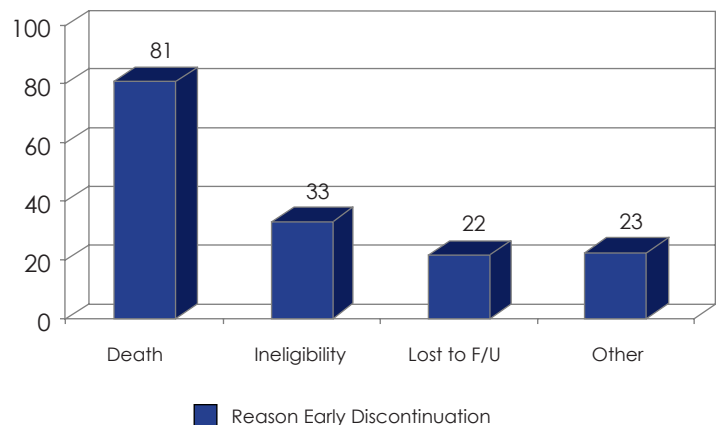
### PAH QuERI Study Progression Updates

Study Progression: Follow up visit date achieved / actual visit completion (13 May, 2008)



### PAH QuERI Early Discontinuation Status

( 22 April, 2008: Total number of patients early terminated: 159 patients )



## Pulmonary Arterial Hypertension

### Diagnostic classification – Differential diagnosis

(Venice, 2003)

#### 1. Pulmonary arterial hypertension

- Idiopathic PAH
- Familial PAH
- Related to:
  - Connective tissue diseases
  - HIV
  - Portal hypertension
  - Anorexigens
  - Congenital heart diseases
- PPHN
- PAH with venule/cap inv (PVOD)

#### 2. PH with left heart disease

- Atrial or ventricular
- Valvular

#### 3. PH with Lung Diseases/Hypoxemia

- COPD
- Interstitial lung diseases
- Sleep-disordered breathing
- Developmental abnormalities

#### 4. PH due to chronic thrombotic and/or embolic disease

- TE obstruction of proximal PA
- TE obstruction of distal PA
- Non thrombotic Pulm embolism

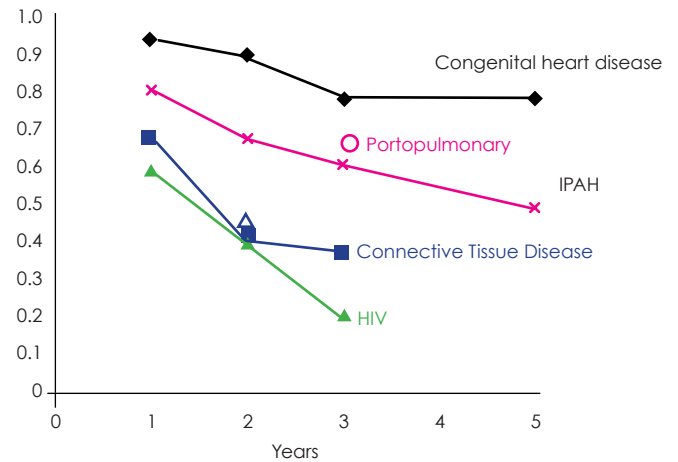
#### 5. Miscellaneous

#### PAH definition:

- mPAP >25 mmHg
- PCW < 15 mmHg
- PVR > 240 dyne·cm/sec-5
- ↑ PAP associated with adverse changes:
  - in the pulmonary vasculature (vasculopathy), and
  - at the level of the right ventricle (hypertrophy)
- absence of lung disease, left-sided heart disease

## Survival in PAH – Influence of Etiology

McLaughlin VV. Chest. 2004;126:785–92S.



### Goals of PAH QuERI:

1. To optimize patient care by providing current guidelines for PAH management through the process of data collection and database analysis.
2. To further close the care gap in PAH management by providing feedback to individual physicians on their style of management compared to the national and regional averages.
3. To follow PAH patients long-term (3 years) and to document outcomes in relation to treatment received.

### PAH QuERI Overview: logistics

**Step 1:** Current guidelines are provided on patient diagnosis after inclusion criteria are satisfied.

- Step 2:**
- a. Practical steps towards confirming diagnosis: essential testing – all patients
  - b. Contingent tests – selected patients.

**Step 3:** Collect data on current patient management while providing guidelines and evidence-based approach.

**Step 4:** Interactive continuing professional development as part of QuERI: implementation of learned principles into practice, i.e. enhancement of care and closure of care gap through physician feedback.

## Preliminary Results

Baseline data reported and signed off at 60 participating US sites on 782 patients enrolled in the PAH QuERI

### Demographics

Review of the baseline clinical characteristics of the enrolled patients, revealed significant preponderance of women and a median age of 55 years. Majority of the patients were symptomatic and many were using supplemental oxygen.

Parameter	Median (25th, 75th), %
Age, y	55 (44, 66)
Female	77%
BMI, kg/m <sup>2</sup>	27.6 (23, 33)
BP, mmHg	SBP 118 (104,130) DBP 70 (61,79)
HR, bpm	81 (72,92)
≥ WHO functional class II	91%
Supplemental oxygen use	44%

### WHO class at enrollment (N=742†)

Review of the functional class demonstrated that majority of the patients were class II or III.

	n (%)
WHO class I	64 (8.6)
WHO class II	290 (39.1)
WHO class III	353 (47.6)
WHO class IV	35 (4.7)

(†) WHO class was unknown in 40 patients (5.1%)

### Initial PAH classification: (N=782)

The etiology of PAH was identified as being associated with an underlying condition in almost 60% of patients, the rest being classified as idiopathic. The most frequent associated condition was connective tissue disease.

	n (%)
Idiopathic	297 (38.0)
Familial	20 (2.6)
Associated conditions	467 (59.7)
Connective tissue dis.	235 (30.1)
Congenital shunt	54 (6.9)
Portal hypertension	30 (3.8)
HIV infection	31 (4.0)
Drug exposure	57 (7.3)
Other	91 (11.6)
Primary venous or capillary involvement	4 (0.5)

## Frequency of ACCP-recommended diagnostic tests

The first table summarizes the frequency with which ACCP-recommended diagnostic tests were deployed. Most of the tests were performed in more than 80% of the enrolled patients, however, V/Q scanning was performed only in 57% of patients, suggesting that the test that can rule out a correctable cause of pulmonary hypertension may not be deployed as optimally as it can be.

The second set of tables summarizes the use of ACCP-recommended blood tests. While most of the tests are deployed in the majority of the patients, HIV testing and CTD screen are not, once again raising the possibility of an incomplete work up of these complex patients.

Test	%
chest x-ray	89
ECG	81
echocardiogram	97
right heart catheterization	90
PFT	83
V/Q scan	57
6-minute walk	76

Test	%
CTD screen	51
HIV test	29
CBC	91
LFT	91
All three tests (CXR, echo, ECG)	74
Either V/Q scan or CT scan	83

## Summary

- Demographics of QuERI reflect typical referral center practice
  - Female predominance
  - Mostly Class II & III
  - 60/40 APAH/IPAH
  - 10% co-existing conditions
  - 87/56% dyspnea/weakness
  - 14% syncope
- Certain diagnostic tests may be underutilized and may impact the patient management

## Conclusions

- A comprehensive and multi-pronged approach to the diagnostic evaluation of PAH is required
- Physicians treating PAH report multiple etiologies
- Certain essential diagnostic tests may be underutilized
- While ACCP guidelines recommend V/Q scanning to exclude correctable causes of PAH, and HIV testing is mandatory in all patients evaluated for PAH, these guidelines are not universally followed
- Given the treatment implications of LHD, a positive HIV test or abnormal V/Q scan, stricter adherence to guidelines may result in more optimal management of these high-risk patients

## ↓ GENERAL NEWS

### **PAH QuERI Educational Initiative -- closure of care gap in PAH diagnosis and management through physician education:**

A web-based individual and confidential feed-back on the baseline data reported has been recently implemented in order to provide each participating physician with diagnostic and treatment information about their own patients enrolled in the PAH QuERI in comparison with the overall performance and site distribution in academic and non academic centers.

### **Study Publication Corner:**

#### **Chest 2007:**

Two abstracts on diagnostic work-up (main author Dr. R. Oudiz) and treatment of PAH (main author Dr. V. McLaughlin) in 517 patients from 52 US specialist physicians, baseline data from the Quality Enhancement Research Initiative, had been presented at CHEST 2007 meeting and published in the abstract supplement for 2007.

#### **ACC 2009:**

Two abstracts on the treatment of PAH baseline data from the QuERI (main author Dr. V. McLaughlin, poster

presentation) and Mortality in patients with PAH in the Modern Era, data from the Quality Enhancement Research Initiative (main author Dr. Mathier, oral presentation) have been accepted for presentation at ACC 2009, March 29-31, 2009 in Orlando, Florida

#### **ATS 2009:**

Tree abstracts on diagnostic work-up (main author Dr. R. Oudiz, treatment of PAH (main author Dr. V. MC Laughlin) and mortality in patients with PAH (main author Dr. M. Mathier), data from the Quality Enhancement Research Initiative, have been accepted for presentation at ATS 2009, May 15-20, 2009, San Diego, California

## ↓ UPCOMING EVENTS

**“Challenges and Controversies in Clinical Cardiology” -- satellite during ACC -- Saturday, March 28, 2009 (12:00 - 2:40 p.m.) at the Rosen Centre Hotel in Junior Ballroom F.**

**“Challenges and Controversies in Clinical Cardiology” satellite during ACC -- Monday, March 30, 2009 (5:30 - 7:00 a.m.) at the Rosen Centre Hotel in Junior Ballroom F.**

## Webcasts on PAH and PAH related topics:

We welcome you to view the accredited webcast presentations at [www.mdprimer.com/opinionupdates](http://www.mdprimer.com/opinionupdates).

### **You Can't Treat It If You Don't Diagnose It: Pulmonary Arterial Hypertension In Scleroderma**

- RICHARD M. SILVER, M.D

### **Pitfalls In The Diagnosis And Management Of Pulmonary Arterial Hypertension**

- LEWIS J. RUBIN, M.D.

### **Detection And Management Of Pulmonary Hypertension In Scleroderma**

- DR. JAMES R. SEIBOLD, MD

### **Antiplatelet Therapy, DES, ICD: Places We Have Lost Our Way And Solutions For The Future**

- ERIC J. TOPOL, MD

### **The Scleroderma Queri - Challenges And Progress**

- DR. JAMES R. SEIBOLD, MD

### **Benefits Of Early Diagnosis And Treatment Of PAH**

- RONALD J. OUDIZ, MD

### **Should Concerns Over Safety Of DES And Efficacy In COURAGE Result In Lowering PCI Use?**

- ERIC J. TOPOL, MD