



# (P)ulmonary (H)ypertension (A)ssessment and (R)eaction of (O)utcomes in (S)cleroderma (Systemic Sclerosis, SSc): PHAROS

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## Abstract

### Background:

Pulmonary arterial hypertension (PAH) and PH secondary to ILD are the leading cause of death and late disease morbidity in SSc. Patients with SSc-PAH have a blunted response to modern therapies by measures of exercise capacity, functional class and survival. The natural history of SSc PAH/PH and its response to treatment is thus still unknown. PHAROS is a multicenter effort by members of the Scleroderma Clinical Trials Consortium. Its objective is to determine the timeline of progression from pre-PAH/PH to diagnosable PAH/PH; to determine the natural history of clinical worsening and the risk factors for early diagnosis.

### Methods:

PHAROS is the prospective observational study of patients with SSc who have PAH/PA < 6 months or who meet criteria for pre-PAH: SPAP by echocardiogram > 35mmHg, DLco<55% of predicted or ratio predicted %FVC/%DLco>1.6. Data are collected bi-annually and include demographics, review of organ involvement, Rx history, medical event history and functional assessment (SHAQ-DI, Borg index, UCSD Dyspnea questionnaire, SF36). Objective data gathering includes: PFT, echocardiogram, 6MWT and right heart catheterization (RHC) parameters. Data are electronically entered by both investigators and subjects.

**Results:** (See table)

### Conclusions:

PHAROS prospectively gathers data to identify tools for early PAH/PH diagnosis, to characterize time to diagnosis of PAH/PH and clinical worsening event rate.

Conclusions continued above:

### Conclusions continued:

Earlier diagnosis of SSc-PAH/PA would offer information relevant to design of prevention trials and lead to strategies that alter the natural history of the disease and clinical worsening event rate. Earlier diagnosis of SSc-PAH/PH would offer information relevant to design of prevention trials and lead to strategies that alter the natural history of the disease.

## Rationale

### Introduction:

- PAH/PH are the leading cause of death and late disease mortality in SSc
- True prevalence and event rate of SSc-PAH/PH is still unknown
- Patients with SSc-PAH have a blunted response to modern therapies by measures of exercise capacity, functional class and survival
- Patients with PH secondary to SSc-ILD have been excluded from pivotal studies

### Purpose of the study:

- PHAROS is a multicenter effort by members of the Scleroderma Clinical Trials Consortium
- One of the objectives is to determine the timeline of progression from pre-PAH/PH to diagnosable PAH/PH
- Another objective is to determine the natural history of clinical worsening
- Determining the risk factors for early diagnosis is another goal of this study

## Methods

### Patients:

- Ongoing enrollment
- Inclusion criteria:
  - \* patients with SSc who have PAH/PH < 6 months or
  - \* patients who meet criteria for pre-PAH/PH:SPAP
- 1. echocardiogram > 35mmHg
- 2. DLco<55% of predicted
- 3. %FVC/%DLco>1.6

### Methods:

- PHAROS is a prospective observational study. Data are collected bi-annually and entered electronically both by investigators and patients in a secure web-based system.

### General data include:

- \* Demographics
- \* Review of organ involvement
- \* Rx history
- \* Medical event history
- \* Functional assessment (SHAQ-DI, Borg index, UCSD Dyspnea questionnaire, SF36)

### Objective data include:

- \* PFT
- \* Echocardiogram
- \* 6MWT and right heart catheterization (RHC) parameters

## Results

- \* 12 SSc centers are actively enrolling and data are preliminary
- \* Of 139 enrollees, 29 had established PAH/PH, 102 have suspected pre-PAH/PH and 8 withdrew consent

	Mean RVSP(mmHg) (% > 35mmHg)	Mean %FVC/%DLco (% > 1.6)	Mean DLco % predicted (% < 55%)	Mean mPAP (RHC) (Number)
PAH/ PH	51.9 (100%)	1.78 (65%)	45.2 (80%)	33.4 (29)
Pre-PAH/PH	42.5 (62%)	1.39 (32%)	65.9 (36%)	20 (12)

Early observations include information about treatment effect on PAH/PH. Of 20 subjects initially on bosentan, 1 progressed to epoprostenol, 2 stopped it secondary to AEs and 10 required additional Rx (sildenafil 8 and iloprost 2).

## Conclusions

- PHAROS prospectively gathers data to develop tools for early PAH/PH diagnosis, to characterize time to diagnosis of PAH/PH and clinical worsening event rate.
- Earlier diagnosis of SSc-PAH/PH would offer information relevant to design of prevention trials and lead to strategies that alter the natural history of disease.