Pulmonary Arterial Hypertension: Causes and Treatments

Published February 12, 2019 by InCrowd, Inc.
Research Objectives

• Understand the current pulmonary arterial hypertension (PAH) patient and treatment landscape
• Explore physician understanding of new treatments in development for PAH and their expectations

Methodology

✓ Method: 8-minute microsurvey via InCrowd
✓ Crowds: US Cardiologists, US Pulmonologists
✓ Sample Size: n=50
✓ Fielding Period: January 30, 2019

Screening Criteria

Qualified respondents are US-based Cardiologists and Pulmonologists who...

• Have at least five PAH patients under their care
• Are aware of products in development for the treatment of PAH
1. PAH patients are differentiated by functional class and cause.
   - Two thirds of PAH patients fall into either Class II (mild limitation of activity) or Class III (marked limitation of activity)
   - The causes of one third of patients’ PAH is either unknown or hereditary

2. Treatment choice is different based on functional class.
   - While only 20% of Class I PAH patients (no limitation of activity) receive oxygen therapy, 71% of Class IV (unable to perform any physical activity, symptomatic at rest) receive this treatment
   - Similarly, endothelin receptor antagonists (ERAs) and prostacyclin analogs jump in usage from Class I to Class IV
   - Class IV patients are also more likely to need atrial septostomy, especially if they are unresponsive to other medical therapy

3. Most physicians feel that increased patient survival, improved health-related quality of life, and improved functional class are the most important clinical trial endpoints for new PAH treatments.
   - Almost half of physicians agree that the ideal mechanism of action (MOA) for new PAH drugs in development should be selective pulmonary vasodilation
Almost half of respondents consider themselves very knowledgeable about products in development for PAH.

Level of Knowledge of PAH Products in Development

<table>
<thead>
<tr>
<th>Extremely Knowledgeable</th>
<th>Very Knowledgeable</th>
<th>Somewhat Knowledgeable</th>
<th>Slightly Knowledgeable</th>
</tr>
</thead>
<tbody>
<tr>
<td>16%</td>
<td>18%</td>
<td>20%</td>
<td>46%</td>
</tr>
</tbody>
</table>

Average # of PAH Patients Treated in Past Three Months
(n=50)

67

How many unique patients with the following conditions are currently under your care? PAH
How would you describe your level of knowledge with products in development for the treatment of PAH?

Most Exciting Developments

- Inhaled Vasodilators/Revatio
- Oral Prostacyclin Analogs/Uptravi/Tyvaso
- ERAs/Letairis/Opsumit ERAs
- ERAs Combination Meds
- PDE5 Inhibitors
- Stem Cell Therapy
- Right Ventricular Assist Device (RVAD)
About a third of PAH patients are classified as functional class II—having mild limitation of physical activity—while another third are classified as functional class III—having marked limitation of physical activity.

<table>
<thead>
<tr>
<th>PAH Patients by Functional Class</th>
<th>(% of Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I—No limitation of usual physical activity</td>
<td>32%</td>
</tr>
<tr>
<td>Class II—Mild limitation of physical activity</td>
<td>12%</td>
</tr>
<tr>
<td>Class III—Marked limitation of physical activity</td>
<td>21%</td>
</tr>
<tr>
<td>Class IV—Unable to perform any physical activity; symptomatic at rest</td>
<td>36%</td>
</tr>
</tbody>
</table>

Of the PAH patients currently under your care, what percentage currently fall into each of the following functional classes?

n=50
In most cases the cause of PAH is either unknown or hereditary.

### Causes of PAH (% of Patients)

- **Idiopathic/Hereditary**: 39%
- **Connective tissue disorders** (e.g. scleroderma and lupus): 18%
- **Congenital heart abnormalities**: 14%
- **Exposure to certain toxins and drugs** (e.g. methamphetamine and cocaine): 9%
- **Chronic liver disease** (e.g. portal hypertension): 7%
- **Infections** (e.g. HIV and schistosomiasis): 5%

Thinking of your current PAH patients under your care, what percent developed PAH due to each of the following causes? Answers do **NOT have to sum to 100** since there can be multiple causes.

n=50
PDE5 inhibitors are the most common treatment for Class I and Class II PAH patients. For more severe functional classified PAH patients, oxygen therapy is most commonly prescribed, however PDE5 inhibitors and ERAs are heavily used as well.

**PAH Treatments by Functional Class**

(\% of Patients)

<table>
<thead>
<tr>
<th>Functional Class</th>
<th>Class I n=43</th>
<th>Class II n=50</th>
<th>Class III n=49</th>
<th>Class IV n=45</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDE5 Inhibitors</td>
<td>23%</td>
<td>38%</td>
<td>47%</td>
<td>46%</td>
</tr>
<tr>
<td>Oxygen Therapy</td>
<td>20%</td>
<td>29%</td>
<td>50%</td>
<td>71%</td>
</tr>
<tr>
<td>Calcium Channel Blockers (CCBs)</td>
<td>16%</td>
<td>18%</td>
<td>18%</td>
<td>19%</td>
</tr>
<tr>
<td>Endothelin Receptor Antagonists (ERAs)</td>
<td>13%</td>
<td>27%</td>
<td>33%</td>
<td>41%</td>
</tr>
<tr>
<td>Prostacyclin Analogs - Oral</td>
<td>9%</td>
<td>13%</td>
<td>21%</td>
<td>28%</td>
</tr>
<tr>
<td>Prostacyclin Analogs - Inhaled</td>
<td>7%</td>
<td>9%</td>
<td>15%</td>
<td>19%</td>
</tr>
<tr>
<td>Soluble Guanylate Cyclase Stimulators (SGCSs)</td>
<td>4%</td>
<td>7%</td>
<td>11%</td>
<td>16%</td>
</tr>
<tr>
<td>Prostacyclin Analogs - IV</td>
<td>3%</td>
<td>9%</td>
<td>17%</td>
<td>28%</td>
</tr>
<tr>
<td>Lung of Heart Transplant</td>
<td>2%</td>
<td>2%</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td>Atrial Septostomy</td>
<td>1%</td>
<td>1%</td>
<td>2%</td>
<td>5%</td>
</tr>
</tbody>
</table>

What percentage of your current PAH patients within functional classes are receiving each of the following treatments? Answers do NOT have to sum to 100 since patients can be on more than one treatment.

*If you do not have patients in a particular functional class, please enter "0" for that column.*

February 12, 2019

Pulmonary Arterial Hypertension: Causes and Treatments | Syndicated Report | Report by InCrowd, Inc.
Patients who are unresponsive or intolerant to therapy are the top candidates for atrial septostomy procedures.

**PAH Patient Types Candidates for Atrial Septostomy**

(% of Mentions)

- **Unresponsive/Intolerant to medical therapy**: 40%
- **Severe PAH**: 10%
- **Palliative**: 8%
- **Right heart failure**: 8%
- **Class IV**: 8%

Q3

Please describe the type of PAH patient who is a good candidate for atrial septostomy?

“Last resort for those not responding to therapy.”

“Severe disease unresponsive to medical therapy.”

“Palliative for severe PAH.”
Over half of respondents say increased patient survival and improved health-related quality of life are highly important clinical trial endpoints for evaluating potential PAH therapies that are in development.

Ranking Importance of Clinical Trial Endpoints
(% Ranked Top Three)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>% Ranked First</th>
<th>% Ranked Second</th>
<th>% Ranked Third</th>
<th>Mean Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase patient survival</td>
<td>42%</td>
<td>12%</td>
<td>10%</td>
<td>3.10</td>
</tr>
<tr>
<td>Improve health-related quality of life</td>
<td>14%</td>
<td>24%</td>
<td>18%</td>
<td>4.12</td>
</tr>
<tr>
<td>Improve functional class</td>
<td>8%</td>
<td>22%</td>
<td>12%</td>
<td>4.32</td>
</tr>
<tr>
<td>Prevent disease progression</td>
<td>8%</td>
<td>18%</td>
<td>14%</td>
<td>4.30</td>
</tr>
<tr>
<td>Better side effect profile</td>
<td>8%</td>
<td>6%</td>
<td>4%</td>
<td>6.22</td>
</tr>
<tr>
<td>Improve 6-minute walk distance (6MWD) to &gt;440 meters</td>
<td>6%</td>
<td>8%</td>
<td>20%</td>
<td>5.02</td>
</tr>
<tr>
<td>Improvement of mean pulmonary arterial pressure</td>
<td>6%</td>
<td>4%</td>
<td>6%</td>
<td>6.26</td>
</tr>
<tr>
<td>Achieve normalization of right ventricular size and function on an echocardiograph</td>
<td>4%</td>
<td>4%</td>
<td>8%</td>
<td>7.18</td>
</tr>
<tr>
<td>Achieve a decrease or normalization of B-type natriuretic peptide</td>
<td>2%</td>
<td>4%</td>
<td></td>
<td>8.08</td>
</tr>
<tr>
<td>Better tolerability</td>
<td>6%</td>
<td>10%</td>
<td>18%</td>
<td>6.40</td>
</tr>
</tbody>
</table>
Selective pulmonary vasodilation is considered the most ideal MOA for treating PAH by almost half of respondents. It’s preferred mostly for fewer side effects and decreased pressure.

**Most Ideal Mechanism of Action for Treating PAH**
(% of Mentions)

- **Selective Pulmonary Vasodilation** 44%
  - Fewer systemic side effects
  - Decrease Pressure (RVP)
  - Prevent right ventricular dysfunction

“Selective pulmonary vasodilator - won’t cause systemic hypertension, less likely for side effects.”

“Pulmonary vasodilation - decrease pressure.”

“Selective PV prevent RV dysfunction yet reduce side effects.”

Q5
When thinking about drugs in development to treat PAH, what is the ideal mechanism of action? Please explain why.
For more information, please contact molly.simpson@incrowdnow.com.

Published February 12, 2019 by InCrowd, Inc.