Clinical Trials Update


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This edition of the Clinical Trials Update was prepared by section editor Dr Levine. It features a review of the baseline characteristics of the REVEAL (Registry to Evaluate Early And Long-term PAH disease management) Registry™.[1] Unlike the clinical trials we have reviewed previously in this section, REVEAL is an important registry of a large cohort of pulmonary arterial hypertension (PAH) patients.

REVEAL was created to define the characteristics, hemodynamics, clinical courses, and management protocols of PAH patients in the US. The goals are to assess differences among WHO Group 1 subgroups, functional status, and hemodynamics, and to provide insight into efficacy of the current diagnostic and treatment strategies that are being practiced as well as help to assess outcomes.

The registry is an observational study of WHO Group 1 PAH patients from 54 pulmonary hypertension (PH) clinics in the US. It was established in March of 2006, and will follow patients for at least 5 years. REVEAL differs from previous registries in several ways. It is the largest PAH registry (2967 patients), and unlike previous cohorts, it includes a substantial number of pediatric patients. The inclusion criteria purposely allowed for patients who do not typically satisfy the traditional hemodynamic classification of PAH (pulmonary artery wedge pressure [PAWP] <15 mm Hg), but who are frequently seen and treated at PH centers. Patients were included if they had PAWP >15/≤18 mm Hg, thus allowing for a comparison between these groups. Enrollment was distributed equally geographically throughout the US. No center enrolled more then 10% of its population.

The study, published February 2010 in *Chest* by Badesch et al, reviews all the baseline characteristics from this registry. Some of the results are summarized here.

Eighty-five percent (2525 patients) of the patients met the traditional hemodynamic definition of PAH. Almost 80% of the patients were female—a much higher percentage than in previous trials. The most common age was between 45 and 54 years, which is older than in previous trials. About half of the patients were diagnosed with idiopathic PAH and half classified as associated PAH (APAH). The most common APAH diagnoses were connective tissue disease and congenital heart disease. Although not thought to be the primary cause of PAH, many of these patients had comorbidities including hypertension, obstructive sleep apnea, and obesity.

At the time of right heart catheterization (RHC), 61% of the patients were functional class III and 12% were functional class IV. At about 25 months after enrollment into the study, 50% were functional class III and 5.6% were class IV. A total of 1335 patients underwent a vasodilator trial and 136 of these were reported as having a significant response. Six-minute walk distance (6MWD) correlated well with functional class; however, there was variability within each class of PAH. Right heart catheterization results did correlate as well.

Interestingly, there was still a significant delay found in the time from symptom onset to diagnostic RHC as seen in previous registries. When the patients did get treated specifically for PAH, a majority of them were treated by pulmonologists (67%).

A total of 2438 patients underwent one or more types of PAH treatment. Four hundred forty-one patients were participating in one of several clinical trials, most of which were open-label trials. Of those being treated with PAH medications, 1008 patients were on 2 or more therapies and 183 were on 3 or more therapies.

Those patients in the "nontraditional" group with the increased pulmonary capillary wedge pressure on RHC tended to be older, more obese, and had a lower 6MWD. This group also had a higher incidence of systemic hypertension, sleep apnea, diabetes mellitus, and renal insufficiency. There were no significant differences between the groups for functional class or PAH treatments at enrollment.

There were 200 pediatric patients enrolled in the study; 67% were female and the mean age at enrollment was 15 years (mean age diagnosis was 8 years). Compared to the adult patients, they had a higher 6MWD, better functional class, higher cardiac index, and fewer comorbidities.

The results from this article characterize the baseline demographics and clinical and treatment strategies at the initiation of the trial. The 5-year data at the end of the study will be useful retrospectively to improve our understanding of the nature of PAH, identify predictors of outcomes, and evaluate relationships among subgroups of PAH and treatment patterns in order to better diagnose and manage our patients. Updates on this ongoing trial will be provided in future editions of this section.

Reference

Badesch DB, Raskob GE, Elliott CG, et al. Pulmonary arterial hypertension: baseline characteristics from the REVEAL Registry. *Chest.* 2009 Oct 16. [Epub ahead of print]

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