CHEST Online Supplement

Results of an Expert Consensus Survey on the Treatment of Pulmonary Arterial Hypertension With Oral Prostacyclin Pathway Agents

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CHEST 2020; 157(4):955-965

 DOI: 10.1016/j.chest.2019.10.043

e-Appendix 1. Literature Search Results

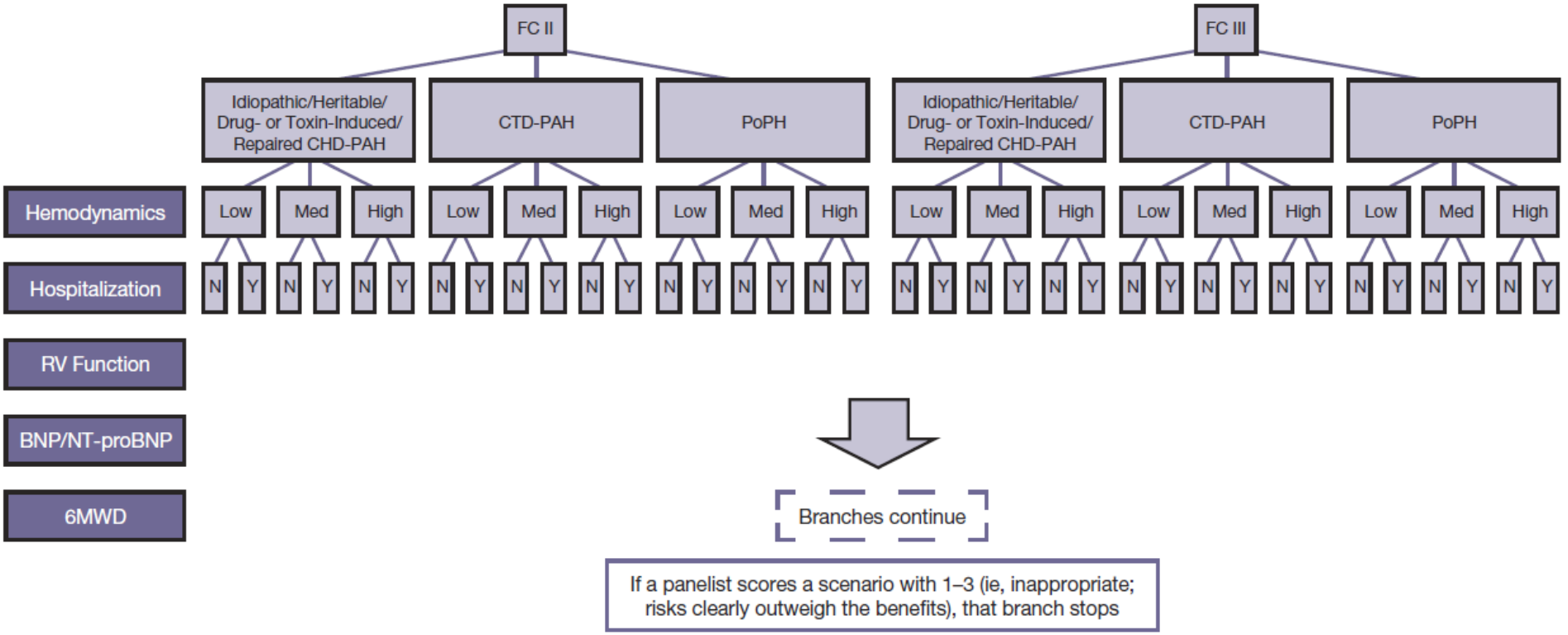
Literature search criteria utilized were ("pulmonary arterial hypertension" OR "pulmonary hypertension") AND (prostacyclin[tw] OR prostanoid[tw] OR PGI2[tw]). The search was limited to English language, adult patients (≥18 years of age), Group 1 pulmonary hypertension (PH; ie, pulmonary arterial hypertension [PAH]), human clinical studies (no animal models or *in vitro* studies), and 10-year time frame from October 1, 2008, through October 1, 2018. The search was augmented with drug prescribing information for prostacyclin pathway agents (PPAs; epoprostanol injection, treprostinil tablets, inhalation, and injection, iloprost inhalation, and selexipag tablets), key articles identified in reference lists outside the search time window, and pivotal trials for oral treprostanil and selexipag. This search produced 477 relevant references containing clinical information and review articles.

These 477 references were analyzed according to titles and abstracts to locate human studies, patients ≥18 years old, Group 1 PH, and topics of interest (timing of PPA initiation, PPA dosing, adverse event management, transitions from parenteral PPAs to oral or inhaled PPAs), resulting in 167 references.

The scope was reduced to focus on oral PPA initiation, resulting in 36 relevant references. Further literature analysis for quality led to inclusion of five references, consisting of two selexipag clinical trials and three oral treprostinil clinical trials:

- Simonneau G, Torbicki A, Hoeper MM, et al. Selexipag: an oral, selective prostacyclin receptor agonist for the treatment of pulmonary arterial hypertension. *Eur Respir J*. 2012; 40(4):874–880.
- Sitbon O, Channick R, Chin KM, et al. Selexipag for the treatment of pulmonary arterial hypertension. *N Engl J Med*. 2015;373(26):2522–2533.
- Jing ZC, Parikh K, Pulido T, et al. Efficacy and safety of oral treprostinil monotherapy for the treatment of pulmonary arterial hypertension: a randomized, controlled trial. *Circulation*. 2013;127(5):624–633.
- Tapson VF, Jing ZC, Xu KF, et al. Oral treprostinil for the treatment of pulmonary arterial hypertension in patients receiving background endothelin receptor antagonist and phosphodiesterase type 5 inhibitor therapy (the FREEDOM-C2 study): a randomized controlled trial. Chest 2013;144(3):952–958.
- Tapson VF, Torres F, Kermeen F, et al. Oral treprostinil for the treatment of pulmonary arterial hypertension in patients on background endothelin receptor antagonist and/or phosphodiesterase type 5 inhibitor therapy (the FREEDOM-C study): a randomized controlled trial. *Chest*. 2012;142(6):1383–1390.

e-Figure 1. Branching Structure of Case Scenarios



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