

Article information: <http://dx.doi.org/10.21037/atm-20-4710>

Manuscript ID: ATM-2020-HF-05(ATM-20-4710)

Manuscript title: Pulmonary Vasodilator Use in Continuous- Flow Left Ventricular Assist Device Management

The authors thank the reviewers and editor for their comments and suggestions. We have addressed the reviewer comments and formatted the manuscript according to Journal guidelines.

Reviewer Comments:

Reviewer A:

Comment 1: Consider referring and adding a line on the article by *Mehra et al* that suggests that ISHLT guidelines for heart transplant listing criteria suggest that adjuvant therapy post-LVAD implantation with phosphodiesterase type 5 inhibitors may be utilized “Mehra MR, Canter CE, Hannan MM, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update. *J Heart Lung Transplantation*. 2016;35:1–23”.

Reply 1: Thank you for the suggestion. The authors have added a statement regarding the use of phosphodiesterase type 5 inhibitors post cfVAD implantation and cited the reference “Mehra MR, Canter CE, Hannan MM, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update. *J Heart Lung Transplantation*. 2016;35:1–23”.

Changes in the text: “The International Society for Heart Lung Transplantation guideline update for heart transplant listing suggests adding PDE5i in patients with persistent PH after LVAD”

Comment 2: Would spell out acronym for SOPRANO Trial the first time used [Study of Macitentan in Patients with Pulmonary Hypertension (PH) Post-Left Ventricular Assist Device (LVAD) Implantation (SOPRANO)]; *ClinicalTrials.gov* Identifier: NCT02554903

Reply 2: Thank you for the suggestion. The acronym SOPRANO was spelled out.

Changes in the text: The SOPRANO (Study of Macitentan in Patients with Pulmonary Hypertension Post-Left Ventricular Assist Device Implantation) trial, the first multi-center randomized placebo-controlled trial to evaluate safety and efficacy of pulmonary vasodilator (macitentan) in patients with precapillary PH post cfLVAD, completed enrollment and pending results.(*ClinicalTrials.gov* Identifier: NCT02554903)

Reviewer B

Comment 1:References should be presented in brackets and within a sentence, instead of superscripts. Please observe this as example of formatting:

<http://atm.amegroups.com/article/view/25992/html>

Reply 1: The format of the references were corrected in the text. The references are presented in brackets and within a sentence.

Changes in the text: An example for correction of presentation of references: “RV function as assessed by right ventricular ejection fraction (RVEF) at rest and exercise is an independent predictor of survival, functional capacity, and need for inotropes or mechanical circulatory support (48-50).”

Comment 2:Line 107: True estimates of PH – HFrEF are (not is).

Reply 2: Thank you for the correction. The sentence was formatted per suggestion.

Changes in the text: Line 127: “**The true estimates of PH in HFrEF are variable** depending on the severity of heart failure, variable definitions used to define PH, presence of comorbidities, study era, and noninvasive versus invasive methods of estimation of PA pressures. Most studies did not differentiate IpcPH and CpcPH”

Comment 3:Line 143: left atrial pressures result (not results).

Reply 3: Thank you for the correction. The sentence was correctly formatted.

Changes in the text: Line 163: “Also, chronically elevated **left atrial pressures result** in pulmonary capillary and arteriolar remodeling with intimal fibrosis, medial hypertrophy, and vascular smooth muscle proliferation.”

Comment 4:Empirically is misspelled in line 381.

Reply 4: Thank you for the correction. The spelling error was corrected.

Changes in the text: Line 408: “Timing of iNO administration **empirically** after induction of anesthesia versus after weaning CPB varies widely across centers and has not been studied.”

Comment 5: Change == in line 435.

Reply 5:== was deleted.

Changes in the text: Line 462: The incidence of RHF was significantly higher in the group not receiving sildenafil establishing the potential for PDE5i use in post cfLVAD patients (87).

Comment 6: Would add a citation for the SOPRANO trial or the clinical trial identifier. The protocol is available as abstract:

Park M, Ewald G, Franco V, Garcia-Ferrer J, Hage A, Horn E, Mandras S, Mathier M, Rame E, Selej M, Frantz R. SOPRANO: Study of Macitentan in Patients with Pulmonary Hypertension (PH) Post-Left Ventricular Assist Device (LVAD) Implantation. Journal of Cardiac Failure. 2016 Aug 1;22(8):S14.

Reply 6: Thank you for the suggestion: The clinical trial identifier was added to the text.

Changes in the text: The SOPRANO (Study of Macitentan in Patients with Pulmonary Hypertension Post-Left Ventricular Assist Device Implantation) trial, the first multi-center randomized placebo-controlled trial to evaluate safety and efficacy of pulmonary vasodilator (macitentan) in patients with precapillary PH post cfLVAD, completed enrollment and pending results(**ClinicalTrials.gov Identifier: NCT02554903**).

Comment 7:There are other spelling and redactions error throughout the article (missing commas, periods), please revise carefully.

Reply 7: Thank you for the suggestions. The authors reviewed the manuscript carefully and corrected the spelling errors and redactions error.