Impact of pre-transplant anti-fibrotic therapy for IPF upon lung transplant outcomes

Todd L. Astor,[1] Hilary J. Goldberg,[2] Laurie D. Snyder,[3] Andrew Courtwright,[4] Ramsey Hachem,[5] Tahuanty Pena,[6] Lorenzo Zaffiri,[3] Gerard J. Criner,[7] Marie M. Budev,[8] Tany Thaniyavarn,[2] Thomas B. Leonard,[9] Shaun Bender,[9] Howard M Lazarus,[10] Aliaa Barakat,[11] Janis Breeze,[12] Peter LaCamera[13]

[1]Division of Pulmonary and Critical Care Medicine, Massachusetts General Hospital, Boston, MA, USA; [2]Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Boston, MA, USA; [3]Division of Pulmonary, Allergy and Critical Care Medicine, Duke University, Durham, NC, USA; [4]Division of Pulmonary, Allergy, and Critical Care, University of Pennsylvania, Philadelphia, PA, USA; [5]Division of Pulmonary and Critical Care, Washington University, St. Louis, MO, USA; [6]Division of Pulmonary, Critical Care and Occupational Medicine, University of Iowa, Iowa City, IA, USA; [7]Department of Thoracic Medicine and Surgery, Temple University, Philadelphia, PA, USA; [8]Respiratory Institute, Cleveland Clinic, Cleveland, OH, USA; [9]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [10]Altavant Sciences, Inc, USA; [11]ILD Collaborative, Boston, MA, USA; [12]Clinical and Translational Science Institute, Tufts University, Boston, MA, USA; [13]Division of Pulmonary, Critical Care and Sleep Medicine, St. Elizabeth's Medical Center, Boston, MA, USA.

INTRODUCTION

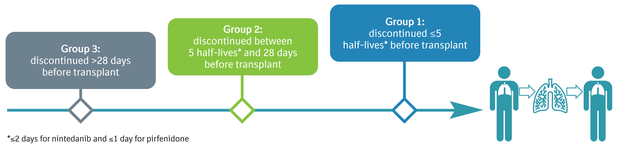
- Nintedanib and pirfenidone are anti-fibrotic medications that slow the progression of idiopathic pulmonary fibrosis (IPF).
- Concern has been raised that anti-fibrotic medications may increase the risk of post-transplant complications such as delayed incisional healing or sternal or anastomotic dehiscence.
- More data are needed on whether continuing antifibrotic therapy until the time of lung transplant increases the risk of complications.

AIM

- To describe variations in intra-operative and post-transplant complications in patients with IPF grouped by the time between discontinuation of anti-fibrotic therapy and lung transplant.

METHODS

- This study (clinicaltrials.gov NCT04316780) included patients with IPF listed for lung transplantation between 1 July 2015 and 30 June 2019, who underwent lung transplantation and had been treated with nintedanib or pirfenidone continuously for ≥90 days at the time of listing for transplantation. Patients who underwent additional interventions (e.g. coronary artery bypass grafting, valve replacement) at the time of their lung transplant were excluded.
- We used data from medical records to assess complications during and in the 6 months after transplant in three groups of patients, based on the time between discontinuation of anti-fibrotic medication and transplant:



*≤2 days for nintedanib and ≤1 day for pirfenidone

- Analyses were descriptive.

CONCLUSIONS

- This observational study indicates variability in the use of anti-fibrotic drugs prior to lung transplant in patients with IPF.
- Descriptive analyses did not suggest differences in the following outcomes depending on when anti-fibrotic therapy was discontinued relative to transplant: need for intra-operative red blood cell transfusion; primary graft dysfunction; surgical wound dehiscence; survival to discharge; length of stay in hospital.
- Anastomotic and sternal dehiscence were only seen in patients whose anti-fibrotic therapy was discontinued <5 medication half-lives prior to transplant; however, these events were infrequent.
- The possibility of disease acceleration and waitlist death with cessation of anti-fibrotic therapy at listing needs to be balanced against the potential for intra- and post-operative complications related to anti-fibrotic therapy.
- The full data set from this study will provide additional insights, but further study will be needed to determine the optimal time to discontinue anti-fibrotic drugs prior to lung transplant.

RESULTS

Patients

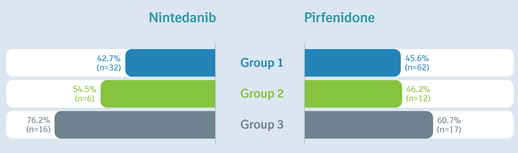
- The analysis included 297 patients from 9 centers (107 taking nintedanib, 190 taking pirfenidone).
- Most patients (nintedanib 70%, pirfenidone 72%) were categorized into group 1.

Patient characteristics at time of listing for transplantation

*Information not available for one patient.

Intra-operative red blood cell transfusion

Percentage of patients who received intra-operative packed red blood cells:



Post-operative outcomes

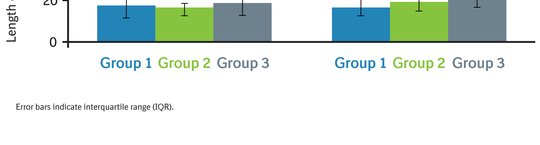
Percentage of patients with primary graft dysfunction:

Percentage of patients with anastomotic dehiscence:

Percentage of patients with surgical wound dehiscence:

Percentage of patients with sternal dehiscence:

Percentage of patients with post-operative return to operating room for lung transplant-related issues prior to discharge:



Percentage of patients who survived to discharge:

Median (IQR) length of hospital stay (days) in patients who survived to discharge (n=283):

Error bars indicate interquartile range (IQR).

ACKNOWLEDGEMENTS
This study was funded by Boehringer Ingelheim Pharmaceuticals, Inc (BIPI). Editorial and formatting assistance was provided by Elizabeth Ng and Wendy Morris of FleishmanHillard Fishburn, which was contracted and funded by BIPI. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE), received no direct compensation for the development of the poster, were fully responsible for all content and editorial decisions, were involved at all stages of development and have approved the final version. BI was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations. Todd L. Astor is a consultant to QxTherapeutics. Peter LaCamera reports no disclosures. Howard M Lazarus was an employee of BIPI at the time that this study was conducted.

INTERACTIVE

https://www.usscicomms.com/respiratory/ATS2020

https://www.usscicomms.com/respiratory/ATS2020/astor

Poster developed for the American Thoracic Society International Conference, 2020.