Role of HMG CoA reductase inhibitors in delaying the development of chronic lung allograft dysfunction post-lung transplant

Amanda Szczepanik, PharmD, BCPS; Jennifer Byrns, PharmD, BCPS; Amanda Hubert, PharmD, BCPS; Clark Benedetti, PharmD, CPP; Hui-Jie Lee, PhD; Laurie Snyder, MD
Duke University Hospital; Durham, North Carolina

Background
• Patients undergoing lung transplantation have reduced survival post-transplant compared to other organ groups with 5-year survival rates estimated to be around 55%
• Overall survival is greatly impacted by the development of chronic allograft dysfunction (CLAD)
• In 2014, the International Society of Heart and Lung Transplant (ISHLT) redefined persistent lung dysfunction. CLAD now serves as an overarching term

Objectives

Primary Objective
• Determine if the use of HMG CoA reductase inhibitors post-lung transplant delays the time to development of CLAD

Secondary Objectives
• Determine the incidence of BOS versus RAS post-transplant
• Determine if the use of statins post-transplant result in improved patient and graft survival rates
• Determine the safety and tolerability of statin use post-transplant

Endpoints

Primary End Point
• Time to development of CLAD by three years post-lung transplant (reported in months)

Secondary End Points
• Incidence of BOS and RAS 3 years post-transplant
• Patient and graft survival at 3 years post-transplant
• Incidence of death due to CLAD
• Incidence of statin discontinuation and reasoning (i.e. CK elevation, rhabdomyolysis, elevation of liver enzymes, myopathy/myalgia)

Methods

Inclusion Criteria
• Underwent an initial bilateral orthotopic lung transplant at Duke University Hospital between 1/1/04-10/31/13
• Has a minimum of 3-year follow up data
• Initiated on a statin within 3 months post-transplant and maintained on therapy for a minimum of 6 months

Exclusion Criteria
• Patients who survived ≤ 90 days
• Recipients with ≤ 5 post-transplant pulmonary function tests (PFTs)
• Re-transplants
• Single orthotopic lung transplant recipients
• Multi-organ transplants
• Hematopoietic stem cell transplant recipients

Statistical Analysis
• Use of propensity score matching or inverse probability of treatment weighting (IPTW) to address treatment selection bias and balance observed covariates between two groups
• Estimate propensity score through logistic regression model

Secondary End points will be summarized with descriptive statistics

Continguous variables will be compared by two-sample t-tests or Mann-Whitney test

Categorical variables will be compared by chi-square test or Fisher’s exact test

Kaplan-Meier survival plot will be created for overall patients and will be stratified by patients with and without statin use

Data Collection and Analysis

The following data points will be collected as a part of this study:
• Baseline demographics
  • Age, gender, end stage lung disease, comorbidities (diabetes, hyperlipidemia, coronary artery disease), transplant date, cold ischemia time, human leukocyte antigen mismatches, percent reactive antibody, immunosuppression regimen (induction and maintenance), CMV serostatus
  • Statin specific information
    • Statin agent used, dose, duration of treatment
    • Tolerability defined as discontinuation due to CK elevation, elevated liver enzymes, rhabdomyolysis diagnosis, self-reported myopathy/myalgia

Subject Identification
• All potential subjects for inclusion will be identified through the use of the Duke lung allograft list. Statin patients will be identified via a query of the Duke Enterprise Data Unified Content Explorer (DEDUCE) database

Secondary End Points
• Diagnosis of CLAD/BOS/RAS and date, patient, and graft survival rates
• In 2014, the International Society of Heart and Lung Transplant (ISHLT) redefined persistent lung dysfunction. CLAD now serves as an overarching term
• Treatment options for CLAD are limited. Targeting known risk factors (i.e. acute allograft rejection, cytomegalovirus (CMV) pneumonitis) are important
• Literature suggests that HMG CoA reductase inhibitors (statins) may play a role in delaying the development of CLAD in lung transplant population through immunomodulatory effects

References

Disclosures
*Authors of this presentation have nothing to disclose concerning possible financial or personal commercial entities that may have a direct or indirect interest in the subject matter of this presentation.