Extracorporeal Photopheresis for the Management of Progressive Bronchiolitis Obliterans Syndrome in Medicare-Eligible Recipients of Lung Allografts (CAG-00324R2)

Status: Completed

Eligibility Criteria

Sex: All
Age: 18 Years and over
This study is NOT accepting healthy volunteers
INCLUSION Criteria for REFRACTORY BOS 1. Age (18 years old or older). 2. Medicare-eligible status 3. Lung transplant recipient (combined organ transplant recipients, e.g. heart-lung or liver-lung or lung re- transplantation recipients are eligible). 4. Patients with a diagnosis of BOS using at least two laboratory based FEV1 values obtained at least three weeks apart that are both at least 20% lower than baseline FEV1 using the International Society for Heart and Lung Transplantation (ISHLT) definition (The average of the two highest FEV1 measurements obtained at least 3 weeks apart after transplantation). The date of Diagnosis of New BOS is the first date of the two FEV1s that were used for the BOS diagnosis. 5. Refractory BOS defined as ongoing decline in FEV1 despite at least one of the following treatments: azithromycin, high-dose steroid, anti-thymocyte globulin, total lymphoid irradiation, sirolimus, or everolimus. 6. At minimum five recorded FEV1 measurements obtained at intervals of at least two weeks apart, over the 9 months preceding study enrollment, of which one FEV1 must be within two weeks prior to enrollment. 7. History of frequent spirometry monitoring defined as having had regular FEV1 measurements within the context of either of the following two options: (1) During the preceding four months prior to enrollment with no time interval between FEV1 measurements that exceeds 8 weeks. (2) During the preceding six months prior to enrollment with no time interval between FEV1 measurements that exceeds 12 weeks. 8. A documented clinical assessment including a physical assessment and Complete Blood Count (CBC) with White Blood Cell Count (WBC) within two weeks prior to enrollment. INCLUSION criteria for NEWLY Diagnosed BOS 1. Age (18 years old or older) 2. Medicare-eligible status. 3. Lung transplant recipient (combined organ transplant recipients, e.g. heart-lung or liver-lung, lung re-transplantation recipients, are eligible). 4. History of close FEV1 monitoring prior to diagnosis of new BOS defined as having had either of the two monitoring approaches: (1) Frequent laboratory based spirometry defined as having had regular FEV1 measurements within the context of either of the following two options: A. During the preceding six months prior to diagnosis of new BOS with no time interval between FEV1 measurements that exceeds 8 weeks. (Participants must be at least 6 months post transplant) B. During the preceding nine months prior to diagnosis of new BOS with no time interval between FEV1 measurements that exceeds 12 weeks (Participants must be at least 9 months post- transplant) (2) Frequent Home Spirometry through the separate IRB approved Standardized Home Spirometry Method sub-protocol. 5. Diagnosis of new BOS (i.e., "new BOS" is defined as within nine weeks of enrollment) based on laboratory-based spirometric FEV1 measurements obtained on at least two separate occasions (i.e., at least 3 weeks apart) that have declined by more than 20% from post-transplant baseline values (i.e., using ISHLT definition). The date of Diagnosis of New BOS is the first date of the two FEV1s that were used for the BOS diagnosis. Inherent to the diagnosis of new BOS is the exclusion of other potential causes of allograft dysfunction such as acute rejection, respiratory tract infection, and airway anastomotic complications. Thus, sites are encouraged to conduct appropriate evaluation for declining allograft function including bronchoscopy with bronchoalveolar lavage (BAL) and lung biopsies if clinically appropriate to exclude other potential causes of allograft dysfunction. 6. Achievement of a statistically significant rate of decline in lung function (FEV1) at the diagnosis of new BOS per the criteria in Section 3.6 as assessed by the following criteria: 1. For patients who are monitored with laboratory based spirometry, at least five recorded FEV1 measurements obtained at intervals of at least two weeks apart, over either the 6 or 9 (i.e., depending on the frequency of spirometry testing) months preceding study enrollment accompanied by a statistically significant ($p<0.05$) rate of decline of FEV1 that exceeds 30 mL/month; or 2. For patients who are monitored with home Spirometry, 4-6 recorded home spirometry FEV1 measurements obtained one week apart, over the 4-6 weeks prior to a confirmed FEV1 variance (i.e., the date of the second of two consecutive FEV1 values below the patient's normal range) along with 4-6 recorded weekly FEV1 measurements obtained after a confirmed variance accompanied by a statistically significant ($p<0.05$) rate of de-cline of FEV1 that exceeds 30 mL/month 7. Documented clinical assessment including a physical assessment and a CBC with WBC within two weeks prior to enrollment. EXCLUSION Criteria (Subjects meeting any one of these criteria will be excluded) 1. Current participation in another clinical treatment trial with an investigational agent used to manage BOS before or after enrollment. 2. Any condition that may interfere with the subject's ability to perform pulmonary function testing. 3. Known allergy or hypersensitivity to pharmacologic agents used during ECP 4. Any condition that would significantly affect the participant's ability to adhere to the protocol, affect interpretation of the study results, or put the participant at unacceptable risk for study-related complications as judged by the referring clinician. This may include a) patients with a specific acute contraindication to receiving ECP due to any acute condition such as new or evolving myocardial infarction or central nervous system disorder, hemodynamic instability or hypovolemia, acute bleeding, respiratory distress. 5. Patients with lupus erythematosus, porphyria cutanea tarda, erythropoietic protoporphyria, variegate porphyria, xeroderma pigmentosum, albinism, or other dermatologic or ocular condition that contraindicates the use of methoxsalen or markedly enhances photosensitivity in the investigator's judgment. 6. Aphakia or absence of ocular lenses 7. Pregnancy (positive pregnancy test

•a urine or blood pregnancy test must be obtained within 2 weeks prior to enrollment in women of childbearing potential) 8. Inability to provide informed consent or to comply with study treatments or assessments (e.g. due to cognitive impairment or geographic distance) 9. Recent (i.e., within 2 weeks prior to enrollment) leukopenia (white blood cell count < 30K/cumm or 3,000/mm3/ or 3.0 109 /L) 10. Patients whose decline in lung function (FEV1) is related to either Restrictive Chronic Lung Allograft Dysfunction (CLAD) or other causes that do not represent BOS such as pneumonia, heart failure, etc. For patients under review for eligibility for ECP for refractory BOS: 11. Patients with a post-transplant baseline FEV1 > 3 liters and most recent FEV1 < 900 mL 12. Patients with a post-transplant FEV1< 3 liters and the most recent FEV1 < 30% of post-transplant baseline 13. Rate of FEV1 decline within the last 6 or 9 months > 300 mL/month. 14. History of receiving ECP therapy within 6 months prior to enrollment. For patients under review for eligibility for RCT: 15. Patients post-transplant treated with any agent that depletes T lymphocytes for In-duction, acute cellular rejection or for any other reason can only be enrolled 12 months after the last dose of these agents assuming they meet enrollment inclusion criteria. T Lymphocyte depleting therapies include (but not limited to):

• monoclonal antibodies such as Alemtuzumab (Campath) that target CD52 T cell receptors

• polyclonal antibodies such as anti-thymocyte globulin (ATG) via immunization of rabbits (rATG) to either human thymocytes or Jurkat cells or via immunization of horses (hATG) to human thymocytes

• Radiation. Anti-B cell agents that do not deplete T lymphocytes such as Rituximab can be used and will not affect eligibility. 16. Any patient who at least 6 months after transplant is treated with an escalated dose of steroids (i.e., prednisone greater than 30 mg/day or that exceeds 900 mg in a 30 day period or equipotent doses of other steroids like Solumedrol) for more than one month for an acute decline in lung function that is suspected to be secondary to acute cellular rejection.

Conditions & Interventions

Interventions:
Combination Product: Extracorporeal Photopheresis (ECP)
Conditions:
Bronchiolitis Obliterans Syndrome (BOS)
Keywords:
Bronchiolitis Obliterans Syndrome, Lung Transplantation, Extracorporeal Photopheresis, Methoxsalen, Clinics and Surgery Center (CSC)

More Information

Description: The primary aims of this revised study are to determine the efficacy and tolerability of ECP for the treatment of either refractory (i.e., in an expanded series of patients within the original prospective cohort Registry) or new (i.e., in a new prospective randomized con-trolled trial sub-study) BOS after lung transplantation in a large patient series.
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Phase: Phase 3
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