April 2014

School of Medicine
Temple University

The Temple Lung Center
3401 N Broad Street
7th Floor Parkinson Pavillion
Philadelphia, PA 19140

Center for Research on Lung Disease

COPD

PIE: Prostaglandin Inhibition for Emphysema

Investigators: Gerard Criner, MD
Coordinators: Dee Fehrle,RN

Description: The Prostaglandin Inhibition for Emphysema (PIE) study will determine if a currently available drug, ibuprofen 600 mg three times daily, can block PGE production in the lower respiratory tract and if this results in improvement in measures of lung repair function. This is a proof-of-concept study that would be for 52 weeks.

Inclusion Criteria: Smoking and ex-smoking control subjects will be recruited from prior COPDGene subjects. All must have consented to be recontacted for additional studies. All must meet the following criteria (as established in their COPDGene database):**Age** > 45 years; **Emphysema** (>5% of voxels <-950 Hounsfield Units determined on the CT scan performed as part of the COPDGene study as quantified at the COPDGene radiology center, i.e. NJH; **COPD of GOLD stage 0, 1, 2 or 3.** (post-bronchodilator FEV1/FVC < 0.7 and post-bronchodilator FEV1 > 35% predicted);**Smoker or ex-smoker** (10 pack years minimum)

Invion Smoking Cessation

Investigator: Aditi Satti, MD
Coordinator: Kim Williams

Description: Primary Objective is to test the hypothesis that 11-15 week treatment with the β adrenergic inverse agonist nadolol will improve smoking cessation in subjects with established COPD (chronic bronchitis dominant) compared to placebo and standard of care. Secondary Objective is to test the hypothesis that 11-15 weeks treatment with nadolol will improve the rate of smoking cessation and safety in subjects with established COPD (chronic bronchitis dominant) compared to placebo (standard of care) at 6 months.

Inclusion Criteria: Active cigarette-smoking males and females between the ages of 18-70 with documented physician-diagnosed COPD (chronic bronchitis dominant), Desire to quit smoking in conjunction with participation in an approved smoking cessation program administered by the participating sites. Pre-bronchodilator FEV1 55 - 70% of predicted; Smoking at least 10 cigarettes per day; Previous failure to quit smoking

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COPD: Lung Function Improvement after Bronchoscopic Lung Volume Reduction with Pulmonx Endobronchial Valves used in Emphysema (LIBERATE)

Investigators: Gerard Criner, MD
Coordinators: Melody Santiago, RN; Gayle Jones, RN; Helga Criner, RN; Jinal Gangar, MBBS, MPH

Description: The Pulmonx Zephyr Endobronchial Valve (EBV) is an implantable bronchial valve intended to decrease volume in targeted regions of the lung. The purpose of this study is to assess the safety and effectiveness of bronchoscopic lung volume reduction (BLVR) using the Pulmonx Endobronchial Valve (EBV) in treated study participants compared to control participants to support a premarket approval application to FDA
Inclusion Criteria: Age 40-75 years; BMI <31.1 Kg/m2 (men) or <32.3 kg/m2 (women); Stable with <20 mg prednisone (or equivalent) daily; Nonsmoking for 4 months prior to screening interview

COPD: RENEW: Lung Volume Reduction Coil for Treatment in Patients with Emphysema Study

Investigator: Gerard Criner, MD
Coordinator: Helga Criner, RN; Jinal Gangar, MBBS, MPH

Description: The RENEW Study is a randomized controlled study evaluating the safety and effectiveness of the Lung Volume Reduction Coil (LVRC) treatment vs. standard medical care. The LVRC is a nitinol coil that is placed bronchoscopically and designed to restore the lung's natural elasticity, improving lung function, quality of life, and exercise tolerance in patients with emphysema
Inclusion Criteria: ≥35 years of age; post-bronchodilator FEV1% ≤45% predicted; Residual Volume (RV) ≥225% predicted; Total Lung Capacity >100% predicted; 6MWT > 140m; stopped smoking for at least 8 weeks – not currently smoking; completed a pulmonary rehabilitation program within 6 months, and/or is on maintenance program

COPD: Otsuka EMPHASIS

Investigators: Francis Cordova, MD
Coordinator: Sylvia C Johnson, RN
Description: Study to assess efficacy of tetomilast 50mcg (inhibits neutrophilic inflammation) in COPD patients
Inclusion Criteria: Age 40-65 years; emphysema on HRCT; FEV1/FVC <0.70 one AECOPD in last year; >20 pack-year smoking history

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COPD: SPIROMICS

Investigators: Gerard Criner, MD
Coordinator: Barbara Macdonald, RN

Description: An investigation of a large number and variety of phenotypic/clinical parameters and biological markers that will be found that enable COPD patients to be divided into homogeneous subgroups for targeted enrollment in future clinical trials.

Inclusion Criteria: Age 40-80 at baseline; Able to tolerate and willing to undergo study procedures; <1 pack-year history for non-smokers; >20 pack year history for smokers; diagnosis of mild-severe COPD; and ability to speak English or Spanish

COPD: LOTT Long Term Oxygen Treatment Trial

Investigator: Gerard Criner, MD
Coordinator: Carla Grabianowski, RN
Description: To demonstrate the effectiveness of supplemental oxygen therapy in COPD patients with moderate hypoxemia at rest
Inclusion Criteria: Age ≥40 years; COPD; ≥ 10 pack-year smoking history; post-bronchodilator FEV1/FVC < 0.70; FEV1% ≤ 70%; oxygen saturation 89-93% at rest, OR oxygen saturation ≥ 94% at rest WITH exercise desaturation to below 90%, OR post-bronchodilator FEV1% > 70% and LOTT physician identifies existing radiographic evidence of emphysema (existing HRTC or CXR can be used); Medicare Parts A & B or Medicare HMO/PPO

COPD: SUMMIT

Investigators: Nathaniel Marchetti, DO; Gerard Criner, MD; Parag Desai, MD
Coordinator: Gayle Jones, RN

Description: A Clinical Outcomes Study to compare the effect of Fluticasone Furoate/Vilanterol Inhalation Powder 100/25mcg with placebo on survival in subjects with moderate Chronic Obstructive Pulmonary Disease (COPD) and a history of or at increased risk for cardiovascular disease
Inclusion Criteria: Outpatient; male or female between 40-80 years of age inclusive at screening a history of ≥10 pack-years of cigarette smoking; post-albuterol FEV1/FVC ratio of <0.70 at screening; FEV1 % ≥ 50% and ≤ 70%. For patients ≥40 years of age any one of the following: coronary artery disease (CAD), peripheral vascular disease (PVD), previous stroke, previous MI, diabetes mellitus with target organ disease; for patients ≥60 years of age: any 2 of the following: hypercholesterolemia, hypertension, diabetes mellitus, peripheral vascular disease

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COPD: Pearl 06

Investigators: **Gerard Criner, MD**
Coordinator: **Gayle Jones, RN**
Description: A Randomized, Double-Blind Chronic Dosing (24 Weeks), Placebo-Controlled, Parallel Group, Multi-Center Study to Assess the Efficacy and Safety of Glycopyrronium and Formoterol Fumarate Inhalation Aerosol, Formoterol Fumarate Inhalation Aerosol and Glycopyrronium Inhalation Aerosol in Subjects With Moderate to Very Severe COPD, Compared With Placebo and Spiriva® Handihaler® (Tiotropium Bromide 18 µg, Open-Label) as an Active Control
Inclusion Criteria: 40 to 80 years of age with a diagnosis of COPD; Females of non-child bearing potential or negative serum pregnancy test; Current or former smokers with a history of at least 10 pack-years of cigarette smoking

Lung Tissue Research Consortium (LTRC)

Investigators: Gerard Criner, MD; Nathaniel Marchetti, DO
Coordinator: Carla Grabianowski, RN; Jinal Ganger MBBS, MPH

Description: Temple Lung Center is participating in the National Heart, Lung and Blood Institute (NHBLI) Lung Tissue Research Consortium (LTRC) to identify patients with COPD and pulmonary fibrosis (idiopathic or connective tissue disease related) and control tissue donors who are scheduled to undergo diagnostic/therapeutic lung resection. The goal is the collection and study of tissues and blood specimens to further understand disease pathogenesis, including the potential roles of lung parenchymal cell apoptosis, immunologic injury and inflammation that may lead to therapies that improve survival and quality of life

COPD Gene Phase 2 Non Smoking Controls

Investigators: Gerard Criner, MD

Coordinator: Carla Grabianowski, RN

Description: 45 – 85 years of age; Non-Hispanic Whites and African Americans; Be a non-smoker (defined as less than 100 cigarettes smoked in a lifetime, less than 52 cigars smoked in a lifetime, and less than 12 oz. of pipe tobacco smoked in a lifetime);Be healthy with no lung problems (FEV_1/FVC and $FEV_1 \geq 0.70$, $FEV_1 \geq 80\%$ predicted)Procedures: Breathing test, blood test, a walking test, CT scan of the chest, questionnaires.The trial consists of 1 – 2 visits to the research facility.

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BI 1012.66: ipratropium bromide and albuterol inhalation spray delivered via the Respimat® inhaler in patients with chronic obstructive pulmonary disease

Investigators: Gerard Criner, MD
Coordinator: Heidi Smith, RN

Description: The primary objective of this study is to compare the efficacy of ipratropium bromide and albuterol inhalation spray delivered via the Respimat® inhaler (Combivent®Respimat®) to that of albuterol sulfate HFA inhalation aerosol and ipratropium bromide HFA inhalation aerosol, measured by lung function, in patients with chronic obstructive pulmonary disease (COPD).
Inclusion Criteria: Outpatients of either sex, 40 years or older, ≥10 pack years of smoking history, with a diagnosis of COPD with FEV1 /FVC <0.70 and post-bronchodilator 30% ≤ FEV1 ≤ 80% of predicted normal FEV1 at Visit 1.

The Prostaglandin Inhibition for Emphysema (PIE)

Investigators: Gerard Criner, MD
Coordinator: Dee Fehrle, RN

Description: The Prostaglandin Inhibition for Emphysema (PIE) study will determine if a currently available therapy, ibuprofen 600 mg three times daily, can block PGE production in the lower respiratory tract and if this results in improvement in measures of lung repair function. This is a proof-of-concept study.

Inclusion Criteria: A total of 140 emphysema subjects will be recruited from prior COPDGene subjects across the four study sites. Smoking and ex-smoking control subjects will be recruited from prior COPDGene subjects. All must have consented to be recontacted for additional studies. All must meet the following criteria (as established in their COPDGene database): **Age** > 45 years; Emphysema (>5% of voxels <-950 Hounsfield Units determined on the CT scan performed as part of the COPDGene study as quantified at the COPDGene radiology center, i.e. NJH);COPD of GOLD stage 0, 1, 2 or 3. (post-bronchodilator FEV1/FVC < 0.7 and post-bronchodilator FEV1 > 35% predicted);Smoker or ex-smoker (10 pack years minimum).

COPD: Inpatient Roflumilast Study

Investigators: **Gerard Criner, MD**
Coordinator: Heidi Smith, RN

Description: Parallel-Group, Prospective, Randomized, Double Blind, Placebo-Controlled trial of Roflumilast 500 ug daily vs. placebo to study the effects of roflumilast in hospitalized COPD patients on Mortality and Re-hospitalization
Inclusion Criteria: Primary diagnosis of AECOPD defined as acute increase in dyspnea, sputum volume, and/or sputum purulence without other identified cause; admission to the hospital <12 hours; patient age >40, < 80 years old; cigarette smoking > 10 pack-years

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Pulmonary Arterial Hypertension

SYMPHONY: A multi-center, open-label, single-arm, Phase 3b study of macitentan in patients with Pulmonary Arterial Hypertension to psychometrically validate the PAH-SYMPACT instrument

Investigator: James Mamary, MD
Coordinator: Gayle Jones

Description: Participants will receive macitentan. It will be used as the drug to see if the PRO can detect any change in quality of life due to macitentan. Using macitentan in this trial will also provide information about its safety in patients with PAH. It will provide information on the effects macitentan has on the PAH-SYMPACT scores. A total of 24 weeks enrollment.
Inclusion Criteria: age 18 or older; symptomatic PAH (WHO) Functional Class (FC) II to IV; PAH belonging to one of the following subgroups of the Dana Point Clinical Classification Group 1: Idiopathic, *or* Heritable, *or*. Drug or toxin induced. Associated with one of the following: Connective tissue disease; Congenital heart disease with simple systemic-to-pulmonary shunt at least one year after surgical repair; HIV infection; diagnosis of PAH by right heart catheterization; (mPAP)≥ 25 mmHg *and* Resting. (PVR)> 240 dyn·s·cm *and* (PCWP) or (LVEDP) ≤ 15 mmHg; 6-minute walk distance (6MWD) ≥ 150 m at Screening.

Pulmonary Arterial Hypertension (PAH) Quality Enhancement Research Initiative (QuERI) Extension Program

Investigator: Sheila Weaver, DO
Coordinator: Gayle Jones, RN

Description: To improve the management of PAH patients through an evidence-based approach. Management of the patient will be according to the treating physician's judgment and in the best interests of the patient. The key variable of impact in this program is assessment of evidence-based therapy and its changes over time
Inclusion Criteria: Male or Female age 18 or older documented diagnosis of PAH; and need for PAH specific treatment

PAH: TYVASO Study

Investigator: Sheila Weaver, DO
Coordinator: Melody Santiago, RN

Description: A post- marketing observational study to assess respiratory tract adverse events in pulmonary arterial hypertension patients treated with Tyvaso (treprostinil) inhalation solution
Inclusion Criteria: Clinical diagnosis of PAH, WHO GROUP I; Prescribed and is currently receiving Tyvaso and/or other FDA-approved therapy for the treatment of PAH

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PAH: IKARIA: IK-7001-PAH-201

Investigator: Gerard Criner, MD
Coordinator: Sylvia C. Johnson, RN

Description: A Phase 2, Placebo Controlled, Double-Blind, Randomized, Clinical Study to Determine Safety, Tolerability and Efficacy of Pulsed, Inhaled Nitric Oxide (iNO) Versus Placebo as Add-on Therapy in Symptomatic Subjects with Pulmonary Arterial Hypertension (PAH)
Inclusion Criteria: Age between 16 and 80 years; confirmed diagnosis of Pulmonary Hypertension Group 1; 6MWD at least 150 meters and no greater than 450 meters; subject is receiving at least one approved PAH therapy and is clinically symptomatic from PAH (e.g., dyspnea on exertion)

PAH/SARCOID: ReSAPH

Investigator: Francis Cordova, MD
Coordinator: Heidi Smith, RN; Maria Rosario, RA

Description: Multi center registry of patients with sarcoidosis associated pulmonary hypertension (SAPH). This is an open label observational study that will characterize the demographics, clinical course, hemodynamics, pulmonary physiology, and disease management of SAPH patients currently under care at the study center versus the newly diagnosed cases of SAPH, comparing the US sites to the non-US sites

PAH: IK-7002-COPD-201

Investigators: A James Mamary, MD
Coordinator: Delores Fehrle, RN

Description: A phase II/III Placebo-Controlled, Double-Blind, Parallel, Randomized, Clinical Dose-Confirming Study Of Pulsed, Inhaled Nitric Oxide (iNO) In Subjects With World Health Organization (WHO) Group 3 Pulmonary Hypertension (PH) Associated With Chronic Obstructive Pulmonary Disease (COPD) On Long Term Oxygen Therapy (LTOT)INHALE 1
Inclusion Criteria: Former smokers with at least 10 pack-years history before study entry and who have stopped smoking ≥ 1 month prior to enrollment ; Age > 40 years, ≤ 80 years; A confirmed diagnosis of COPD (GOLD) criteria; FEV1/FVC < 0.7 and a FEV1 < 60% predicted; Receiving LTOT for ≥ 3 months and ≥ 10 hours per day as determined by history

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Idiopathic Pulmonary Fibrosis

ART-IPF: Autoantibody Reduction Therapy for Patients with Idiopathic Pulmonary Fibrosis

Investigator: Gerard Criner, MD
Coordinator: Barbara Macdonald

Description: multicenter, randomized, double-blind, Phase II clinical trial to determine effects of rituximab on selected relevant immunological parameters of IPF patients, in comparison to effects of placebo alone. The study will be for 9 months.
Inclusion Criteria: Diagnosis of IPF, not established >5 years from the enrollment date, that fulfills ATS/ERS Consensus Criteria; Age 50-85 years old; Ambulatory; Presence of autoantibodies against HEp-2 cells at plasma titrations of >1:20, the assay for the primary endpoint.

BI 1199.187

Investigator: Francis Cordova, MD
Coordinator: Barbara Macdonald, RN

Description: A double blind randomized placebo controlled trial evaluating the effect of oral nintedanib 150 mg twice daily on high resolution computerized tomography quantitative lung fibrosis score, lung function, six minute walk test distance and St. George's Respiratory Questionnaire after twelve months of treatment in patients with Idiopathic Pulmonary Fibrosis with continued evaluations over a period of up to eighteen months.
Inclusion Criteria: (FVC) ≥ 50% of predicted; (DLCO) 30-79%; Confirmed diagnosis of IPF by HRCT or lung biopsy taken within 24 months

PIPF-031: A Treatment Protocol to Allow Patients in the US with Idiopathic Pulmonary Fibrosis Access to Pirfenidone

Investigator: Francis Cordova, MD
Study Coordinator: Melody Santiago

Description: This is a multi-center treatment protocol to allow patients in the US with IPF access to treatment with pirfenidone. Patients will be enrolled in the program for up to 18 months from the initiation of the program or pirfenidone becomes commercially available in the US or the sponsor terminates the program.
Inclusion Criteria: clinical and radiographic diagnosis of IPF including the presence of UIP pattern or possible UIP pattern on historical HRCT (ATS 2011); % FVC≥50% and %DLco≥30%; adherence to program treatment (pirfenidone)

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Safety and Efficacy of BMS-986020 in Subjects with Idiopathic Pulmonary Fibrosis

Investigators: **Francis Cordova, MD**
Coordinator: **Sylvia C. Johnson, RN**

Description: A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study of the Safety and Efficacy of BMS-986020 in Subjects with Idiopathic Pulmonary Fibrosis pulmonary fibrosis
Inclusion Criteria: Are between the ages of 40 and 80 years; Have a body mass index of 18 to 35; Have clinical symptoms consistent with IPF for 12 months or more before screening or at any time in the past; Have first received a diagnosis of IPF at least 6 months and no more than 48 months before randomization; Have a diagnosis of usual interstitial pulmonary fibrosis (UIP) or IPF by HRCT or surgical lung biopsy (SLB)

IPF: Evaluating the Efficacy of Tralokinumab in Adults with Idiopathic Pulmonary Fibrosis (MedImmune)

Investigators: **Francis Cordova, MD**
Coordinator: **Barbara Macdonald, RN**

Description: A Phase II dose-ranging study to evaluate the safety and effectiveness of multiple-doses of tralokinumab on pulmonary function in adults with mild to moderate idiopathic pulmonary fibrosis

Inclusion Criteria: Age 50-79 years; IPF diagnosis for ≤ 4 years prior to Visit 1 (screening); Mild to moderate IPF to include all of the following at screening: FVC ≥ 50% and ≤ 90% predicted normal ; PaO2 of ≥ 55 mmHg on room air or 50 mmHg at high altitude (> 1,500 meters), SpO2 of ≥ 90% on room air at rest; DLCO ≥ 30% and ≤ 90% predicted normal ; able to walk ≥ 100 meters unassisted ; Body weight 45-145 kg

IPF: RAINIER

Investigators: **Francis Cordova, MD**
Coordinator: **Melody Santiago, RN**

Description: A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Assess the Efficacy and Safety of GS-6624 in subjects with Idiopathic Pulmonary Fibrosis
Inclusion Criteria:
Male or female age 45 to 85 with a diagnosis of IPF within 3 years prior to screening confirmed by HRCT or Surgical Lung Biopsy; 6MWD ≥ 50 meters: use of ≤ 6 L/min supplemental O_2 is required for all subjects; Able to maintain oxygen saturation of ≥ 89% while breathing room air at rest; Negative serum pregnancy test

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IPF: Hoffmann-La Roche Lebrikizumab

Investigators: **Irene Swift, MD**
Coordinator: **Gayle Jones, RN**

Description: A Phase 2, Randomized, Double-Blind, Placebo-Controlled study to assess the efficacy and safety of lebrikizumab in patients with Idiopathic Pulmonary Fibrosis
Inclusion Criteria:
Age≥40 years at Visit 1; IPF diagnosis within 4 years; Central review assessment of a screening HRCT; All patients who have undergone a SLB as part of their initial workup should have pathology slides sent in for SLB central review assessment; FVC≥40%and ≤90% of predicted at screening; DLCO ≥25% and≤90% of predicted at screening; Ability to walk ≥100 meters unassisted in 6 minutes

ASTHMA

ASTHMA: KIA Study

Investigators: **Kartik Shenoy, MD**
Coordinator: **Sylvia Johnson, RN**

Description: A 30 to 34 week, treatment randomized, double-blind, placebo-controlled study of the effects of cKit inhibition by imatinib in patients with severe refractory asthma (KIA)

Inclusion Criteria: Patients 18-65 years of age, diagnosed with asthma for at least 1 year; Refractory asthma, defined as asthma not completely controlled in the past 3 months despite continuous treatment with high-dose inhaled corticosteroids (ICS) and at least one additional controller medication; Prebronchodilator FEV1 ≥ 40% predicted; Methacholine PC20 ≤ 10 mg/ml; > 80% compliance with PEF recording and diary recording during the run in period

Inpatient Studies/Other

SEPSIS: EUPHRATES

Investigator: **Nathaniel Marchetti, DO**
Coordinator: **Sally Boyle Quinn, RN**

Description: To assess the safety and efficacy of polymixin B hemoperfusion in patients with septic shock and high levels of endotoxin
Inclusion Criteria: Hypotension requiring vasopressors, suspected infection; endotoxin activity assay ≥ 0.6; > 1 new onset organ dysfunction