Idiopathic Pulmonary Fibrosis: An Update and New Clinical Trials
Yolanda Mageto, M.D., M.P.H.

It has been a while since IPF was discussed in this forum and there are some new and exciting updates to report. For those unfamiliar with the disease here is a quick review. Idiopathic Pulmonary Fibrosis or IPF as it is more commonly known is a uniformly fatal lung disease of persistent, progressive scarring of the lung. The disease typically affects those between ages 45-80. The most common symptom is progressive shortness of breath. Unfortunately because this disease occurs in an age group where this may be part of the normal aging process it is often overlooked until the shortness of breath is rather extreme and cannot be attributed to the aging process. Other symptoms include fatigue, a dry cough. Weakness, poor appetite, weight loss, and general debility, but many have no symptoms for years.

The gold standard for diagnosing this disease remains an open lung biopsy which requires general anesthesia and hospitalization. The good news is that we can make a fairly accurate diagnosis most of the time based on a constellation of symptoms and clinical findings such as pulmonary function studies, CT scan and six minute walk test. While there is no cure there is hope. Pirfenidone a medication that has been studied for this purpose for years just released the results of its recent clinical trial. It was a positive study that suggests the drug may indeed slow the rate of progression of this disease and it may soon be available in the United States. A second drug Nintedanib also seems to hold promise for possibly slowing the rate of disease. The results of this study will be released soon. These drugs still have to go through the FDA and subsequent manufacturing so it will be a while before they are available if approved.

The VLC continues to have clinical trials as we have not yet found a cure and one drug does not necessarily work for all. We currently have 3 actively enrolling trials for IPF. All three are double blinded and placebo controlled trials. This means patients enrolled will receive either active drug or placebo.

Fibrogen tests the effectiveness of a monoclonal antibody FG-3019 directed against Connective Tissue Growth Factor (CTGF), a hormone-like material made in the lung that is believed to promote lung fibrosis. The drug is given intravenously every 3 weeks for one year.

RIFF study by Roche/Genentech testing the efficacy and safety of Lebrikizumab a monoclonal antibody directed against interleukin 15 a cytokine that is believed to promote lung fibrosis. The drug is given subcutaneously every 4 weeks for a year.

BMS-986020: Safety and efficacy of a lysophosphatidic acid receptor antagonist in IPF. Animal studies have suggested that blocking these receptors will slow the rate of fibrosis. The drug is in tablet form and taken daily for 26 weeks.

More information about all of these trials can be obtained through the Vermont Lung Center or at www.clinicaltrials.gov. We are delighted to see the progress made in the last 3 years since we last reported on this topic and are hopeful that we will continue forward in the search for a cure.
Lung cancer screening offers hope for improved survival through early detection, finding small tumors before they spread to regional lymph nodes or outside of the chest. The strategy of early detection is well-known for breast cancer and colon cancer, where mammograms or colonoscopy are used to find small tumors that would not be felt or cause attention from symptoms. New results from screening trials provide evidence that deaths due to lung cancer can be reduced through early detection.

Lung is the most common cancer site and by far the most common cause of cancer deaths in Vermont, with more deaths due to lung cancer than colon, breast, and prostate combined. Lung cancer is found equally in men and women, with an average age of 68 years at diagnosis.

<table>
<thead>
<tr>
<th>CANCER SITE</th>
<th>VERMONT CASES PER YEAR</th>
<th>VERMONT DEATHS PER YEAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Cancer</td>
<td>530</td>
<td>382</td>
</tr>
<tr>
<td>Prostate Cancer (men)</td>
<td>506</td>
<td>61</td>
</tr>
<tr>
<td>Breast Cancer (women)</td>
<td>514</td>
<td>83</td>
</tr>
<tr>
<td>Colon Cancer</td>
<td>306</td>
<td>116</td>
</tr>
</tbody>
</table>

Most cases of lung cancer occur in people who are current or former smokers, but about 15% of lung cancers occur in people who never smoked tobacco. Most smokers have quit before their lung cancer is found, but the high risk continues for at least 15 – 20 years. Only one-third of lung cancers are at an early stage (I or II) when diagnosed where surgery might cure the disease. About two-thirds of cases are at an advanced stage (III or IV) when diagnosed, and while chemotherapy, radiation therapy, and other measures prolong life and reduce symptoms, these treatments rarely offer cure. Headlines announced a 20% reduction in lung cancer mortality when the results of the National Lung Screening Trial were published in 2011. Subjects at high risk for lung cancer were assigned at random to receive annual screening either with a plain chest X-ray (previously shown not to improve outcomes) or with a low-dose non-contrast computed tomography scan of the chest (LDCT scan). The radiation exposure from the LDCT scan is very low, about one-third the annual environmental exposure in Vermont, 8-10 airline flights across the country, or 10 plain chest X-rays. More than 52,000 subjects were screened for 3 years and then observed for an additional 4 years. The number of cancers detected was increased in the LDCT scan group.

INTERESTED IN VOLUNTEERING?

Things to know.

1) The Vermont Lung Center staff is responsible for making sure you know what is expected of you in regards to the study.

2) Once the study is explained to you, you will be asked to read and sign an “Informed Consent”. This form is designed to explain everything you need to know about the study.

3) Studies may be therapeutic (involving observation of lung function). However The Vermont Lung Center can make no claims that your involvement in a research study will improve your condition.

4) Compensation may or may not be provided to you for your involvement in a study. If compensation is provided, it is meant to cover your time and expenses incurred—it does not constitute employment.

If you are interested in volunteering for a research study, please call us at (802) 847-2193.
**ASHTMA**

**LASST** (Long-acting Beta Agonist Step Down Study),
Volunteers: Asthmatics ages 12 and over
11 visits -- Compensation: $75 per visit

**SAPS (Smoking Asthmatics Cohort Study),**
Volunteers: Asthmatics Smokers ages 18-50
2 visits – Compensation: up to $175

**CHAIR** (Study of Changes in Allergic Inflammation and Airway Remodeling During Bariatric Surgery),
Volunteers: Asthmatics ages 18 and older having bariatric surgery
2 visits – Compensation: $25 per visit

**DUOX** (Epithelial Duox1, IL-33, and Allergic Inflammation),
Volunteers: Asthmatics and Non-Asthmatics ages 18-65
1 visit – Compensation: $25

**ELVAS** (Assessing the Effects of Lung Volume and Time on Airway Responsiveness in Asthmatic Subjects),
Volunteers: Asthmatics and Non-Asthmatics ages 18-65
3 visits – Compensation: Up to $200

**NAC** (Effect of BMI on Allergic Responses),
Volunteers: Asthmatics ages 18-65 and allergic to dust mites
3-4 visits – Compensation: up to $200

**IDIOPATHIC PULMONARY FIBROSIS (IPF) STUDIES**

**RIFF** (A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Lebrikizumab in Subjects with IPF)
Volunteers: Age 40 and over, with IPF
Up to 34 visits over a 2 years – Travel compensation over 100 + mi.

**Fibrogen-067** (A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of FG-3019 in Subjects with IPF),
Volunteers: Age 40-80 years inclusive with IPF
Up to 38 visits over a 2 year period – Compensation: up to $3,800

**BMS** (Safety and Efficacy of A Lysosphatidic Acid Receptor Antagonist in Idiopathic Pulmonary Fibrosis A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study of the Safety and Efficacy of BMS-986020 in Subjects with IPF),
Volunteers: age 40 and over with IPF
14 visits for a total of 30 weeks – Compensation: $1,025 – 1,275

**CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)**

**FOREST** (A 52-week, Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study Evaluating Effect of Roflumilast 500 µg on Exacerbation Rate in Subjects with Chronic Obstructive Pulmonary Disease (COPD) Treated with a Fixed-Dose Combination of Long-Acting Beta Agonist and Inhaled Corticosteroid (LABA/ICS)),
Volunteers: 40 Years + with COPD
8 Visits over 1 year – Compensation: Up to $2000, AND Advair 250/50 or Symbicort 160/4.5 and Albuterol provided

**PULMONARY ARTERIAL HYPERTENSION**

**DLCO-PAH** (Changes in the Diffusion Capacity for Carbon Monoxide (DLCO) in Response to Vasodilator Therapy in Patients with Pulmonary Arterial Hypertension),
Volunteers: Patients with Pulmonary Arterial Hypertension
3 Visits – Compensation: None

**CYSTIC FIBROSIS**

**Gilead (A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of Aztreonam for Inhalation Solution (AZLI) in a Continuous Alternating Therapy (CAT) Regimen of Inhaled Antibiotics for the Treatment of Chronic Pulmonary Pseudomonas aeruginosa Infection in Subjects with Cystic Fibrosis),**
Volunteers: People with CF hospitalized in the past year
9 visits over an 8 month period – Compensation: Up to $675

**A Phase 2, Randomized, Multicenter, Double-Blind, Placebo-Controlled Study to Evaluate Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of VX-661 in Combination with Ivacaftor for 12-Weeks in Subjects with Cystic Fibrosis, Homozygous for the 508del-CFTR Mutation,**
Volunteers: People with CF 18 Yrs and over, Homozygous for the F508del-CFTR Mutation
9 visits over a 4 month period – Compensation: Up to $400

**STUDIES CONDUCTED IN THE INTENSIVE CARE UNIT** – Pharmaconutrients as Therapies for Critical Illness: Zinc in Severe Sepsis
Who: Critically ill patients with severe sepsis and requiring mechanical ventilation.
One week of IV infusions of zinc or placebo three times a day.

**A Randomized Double-Blind Placebo-Controlled Trial of Ganciclovir/Valganciclovir for Prevention of Cytomegalovirus Reactivation in Acute Injury of the Lung and Respiratory Failure (GRAIL)**
Who: Patients who are critically ill and have acute lung injury (ALI) or respiratory failure.
Enrolled participants will receive an antiviral medication called ganciclovir or a placebo, either through an IV or orally for 14-28 days

**Telemedicine as a Tool for Family Conferences in Critically ill Patients with High Risk of Imminent Death**
Who: Patients who are critically ill, at increased risk of death and being considered for transfer to FAHC for further treatment.
Family members will participate in a conference with medical personnel from FAHC prior to the patient’s transfer to evaluate the delivery of information via telemedicine (video conference)

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**Interested in volunteering?**

Please call

802-847-2193
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Lung Cancer Screening

Gerald Davis, M.D.

(1,060 vs 941), but the number of deaths was decreased significantly (346 vs 572). The decrease in deaths was clearly due to a higher proportion of patients with early stage disease. Approximately 2 new lung cancers were found for every 100 subjects screened. None-the-less, many subjects showed a CT scan with a small abnormality that might be lung cancer but proved not to be – a “positive” scan that was false. A similar proportion of “falsely positive” results are found with screening mammography. Subjects with a suspicious abnormality would be called back for a repeat LDCT scan in 3 – 6 months, the rest continuing with annual screening.

The U.S. Preventive Services Task Force issued a recommendation in favor of lung cancer screening in December 2013. The approval by this government agency should mandate payment by health insurance carriers. The people considered at highest risk are those eligible for screening: subjects 55-80 years of age who have smoked 30 pack-years (1 pack per day for 30 years or the equivalent) and are current or former smokers who quit for 15 years or less. Lung cancer screening is beginning now at Fletcher Allen Health Care and other hospitals in our region. If someone is eligible, annual screening LDCT scans can be ordered by their primary care physician. The time has come.