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# Is it Idiopathic Pulmonary Fibrosis? Diagnostic Challenges and Treatment

An Industry-Organized Symposium at the ATS 2016 International Conference

May 15, 2016

6:30 PM – 8:30 PM Dinner/Symposium

Marriott Marquis San Francisco • Marriott Marquis in Golden Gate B  
San Francisco, CA

## PROGRAM OBJECTIVE

The process of identifying, diagnosing, and treating idiopathic pulmonary fibrosis (IPF) will be explored by a multidisciplinary panel of expert faculty, including a pulmonologist, radiologist, and a pathologist. The use of OFEV® (nintedanib) for the treatment of patients with IPF will also be reviewed

## DISTINGUISHED FACULTY

### Marilyn K. Glassberg, MD

Professor of Medicine, Surgery,  
and Pediatrics  
University of Miami Miller School of Medicine

### Sudhakar Pipavath, MD

Associate Professor, Radiology  
University of Washington

### Mark Rumbak, MD

Professor, College of Medicine,  
Internal Medicine  
University of South Florida

### Kirk Jones, MD

Professor, Pathology  
UCSF School of Medicine

## PROGRAM OVERVIEW

Join us for a multidisciplinary panel discussion about IPF featuring faculty from three disciplines, each of whom plays a key role in the diagnosis and treatment of patients with IPF. Participants will have several opportunities to ask the experts questions during question and answer sessions throughout the program. Interactive content will include topics related to the diagnosis of IPF and treatment with OFEV as recommended by the 2015 American Thoracic Society (ATS) 2015 joint ATS, ERS, JRS, ALAT Guidelines.<sup>1a</sup>

<sup>a</sup>This is a conditional recommendation, meaning that the majority of patients will want the suggested intervention, but many will not, and different choices will be appropriate for individual patients, according to his or her values and preferences.<sup>1</sup>

1. Raghu G et al; on behalf of the ATS, ERS, JRS, and ALAT. *Am J Respir Crit Care Med.* 2015;192(2):238-248.

## PROGRAM AGENDA

## FACULTY

6:30 – 7:00 PM	Program registration and reception
7:00 – 7:45 PM	Disease state panel discussion - Marilyn Glassberg, Sudhakar Pipavath, Kirk Jones
7:45 – 8:30 PM	Efficacy and safety of OFEV for IPF - Mark Rumbak

A non-CME educational program sponsored by Boehringer Ingelheim Pharmaceuticals, Inc., open to all ATS 2016 International Conference attendees.

Aspects of this program may be reportable under the Physicians Payment Sunshine Act. Attendance at this promotional program is limited to healthcare professionals.

## IMPORTANT SAFETY INFORMATION WARNINGS AND PRECAUTIONS

### Hepatic Impairment

- OFEV is not recommended in patients with moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment. Patients with mild hepatic impairment (Child Pugh A) can be treated with a reduced dosage (100 mg twice daily). Consider treatment interruption or discontinuation for management of adverse reactions.

Please see additional Important Safety Information on the reverse side and enclosed full Prescribing Information, including Patient Information.



## IMPORTANT SAFETY INFORMATION AND INDICATION WARNINGS AND PRECAUTIONS

### Elevated Liver Enzymes

- OFEV was associated with elevations of liver enzymes (ALT, AST, ALKP, and GGT) and bilirubin. Liver enzyme increases were reversible with dose modification or interruption and not associated with clinical signs or symptoms of liver injury. The majority (94%) of patients with ALT and/or AST elevations had elevations <5 times ULN. The majority (95%) of patients with bilirubin elevations had elevations <2 times ULN.
- Conduct liver function tests prior to treatment, monthly for 3 months, and every 3 months thereafter, and as clinically indicated. Monitor for adverse reactions and consider dosage modifications, interruption, or discontinuation as necessary for liver enzyme elevations.

### Gastrointestinal Disorders

#### Diarrhea

- Diarrhea was the most frequent gastrointestinal event reported in 62% versus 18% of patients treated with OFEV and placebo, respectively. Events were primarily mild to moderate intensity and occurred within the first 3 months. Diarrhea led to permanent dose reduction in 11% and discontinuation in 5% of OFEV patients versus 0 and <1% in placebo patients, respectively.
- Dosage modifications or treatment interruptions may be necessary in patients with diarrhea. Treat diarrhea at first signs with adequate hydration and antidiarrheal medication (e.g., loperamide), and consider treatment interruption if diarrhea continues. OFEV treatment may be resumed at the full dosage (150 mg twice daily), or at the reduced dosage (100 mg twice daily), which subsequently may be increased to the full dosage. If severe diarrhea persists, discontinue treatment.

#### Nausea and Vomiting

- Nausea was reported in 24% versus 7% and vomiting was reported in 12% versus 3% of patients treated with OFEV and placebo, respectively. Events were primarily of mild to moderate intensity. Nausea and vomiting led to discontinuation of OFEV in 2% and 1% of patients, respectively.
- If nausea or vomiting persists despite appropriate supportive care including anti-emetic therapy, consider dose reduction or treatment interruption. OFEV treatment may be resumed at full dosage or at reduced dosage, which subsequently may be increased to full dosage. If severe nausea or vomiting does not resolve, discontinue treatment.

**Embryofetal Toxicity:** OFEV can cause fetal harm when administered to a pregnant woman and patients should be advised of the potential risk to a fetus. Women should be advised to avoid becoming pregnant while receiving OFEV and to use effective contraception during treatment and at least 3 months after the last dose of OFEV. Verify pregnancy status prior to starting OFEV.

**Arterial Thromboembolic Events:** Arterial thromboembolic events were reported in 2.5% of OFEV and 0.8% of placebo patients, respectively. Myocardial infarction was the most common arterial thromboembolic event, occurring in 1.5% of OFEV and 0.4% of placebo patients. Use caution when treating patients at higher cardiovascular risk including known coronary artery disease. Consider treatment interruption in patients who develop signs or symptoms of acute myocardial ischemia.

**Risk of Bleeding:** OFEV may increase the risk of bleeding. Bleeding events were reported in 10% of OFEV versus 7% of placebo patients. Use OFEV in patients with known risk of bleeding only if the anticipated benefit outweighs the potential risk.

**Gastrointestinal Perforation:** OFEV may increase the risk of gastrointestinal perforation. Gastrointestinal perforation was reported in 0.3% of OFEV versus in 0% placebo patients. Use caution when treating patients who have had recent abdominal surgery. Discontinue therapy with OFEV in patients who develop gastrointestinal perforation. Only use OFEV in patients with known risk of gastrointestinal perforation if the anticipated benefit outweighs the potential risk.

### ADVERSE REACTIONS

- Adverse reactions reported in ≥5% of OFEV patients included diarrhea, nausea, abdominal pain, liver enzyme elevation, vomiting, decreased appetite, weight decreased, headache, and hypertension.
- The most frequent serious adverse reactions reported in OFEV patients were bronchitis and myocardial infarction. The most common adverse events leading to death in OFEV patients versus placebo were pneumonia (0.7% vs. 0.6%), lung neoplasm malignant (0.3% vs. 0%), and myocardial infarction (0.3% vs. 0.2%). In the predefined category of major adverse cardiovascular events (MACE) including MI, fatal events were reported in 0.6% of OFEV versus 1.8% in placebo patients.

### DRUG INTERACTIONS

- **P-glycoprotein (P-gp) and CYP3A4 Inhibitors and Inducers:** Coadministration with oral doses of a P-gp and CYP3A4 inhibitor, ketoconazole, increased exposure to nintedanib by 60%. Concomitant use of potent P-gp and CYP3A4 inhibitors (e.g., erythromycin) with OFEV may increase exposure to nintedanib. In such cases, patients should be monitored closely for tolerability of OFEV. Management of adverse reactions may require interruption, dose reduction, or discontinuation of therapy with OFEV. Coadministration with oral doses of a P-gp and CYP3A4 inducer, rifampicin, decreased exposure to nintedanib by 50%. Concomitant use of P-gp and CYP3A4 inducers (e.g., carbamazepine, phenytoin, and St. John's wort) with OFEV should be avoided as these drugs may decrease exposure to nintedanib.
  - **Anticoagulants:** Nintedanib may increase the risk of bleeding. Monitor patients on full anticoagulation therapy closely for bleeding and adjust anticoagulation treatment as necessary.
- ### USE IN SPECIFIC POPULATIONS
- **Nursing Mothers:** Because of the potential for serious adverse reactions in nursing infants from OFEV, advise women that breastfeeding is not recommended during treatment.
  - **Reproductive Potential:** OFEV may reduce fertility in females of reproductive potential.
  - **Smokers:** Smoking was associated with decreased exposure to OFEV, which may affect the efficacy of OFEV. Encourage patients to stop smoking prior to and during treatment.

**OFEV is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).**

**Please see enclosed full Prescribing Information, including Patient Information.**

