PRODUCT UPDATE

January 2016

This supplement was funded and developed by Boehringer Ingelheim Pharmaceuticals, Inc., makers of OFEV®

OFEV® (nintedanib) capsules 150mg

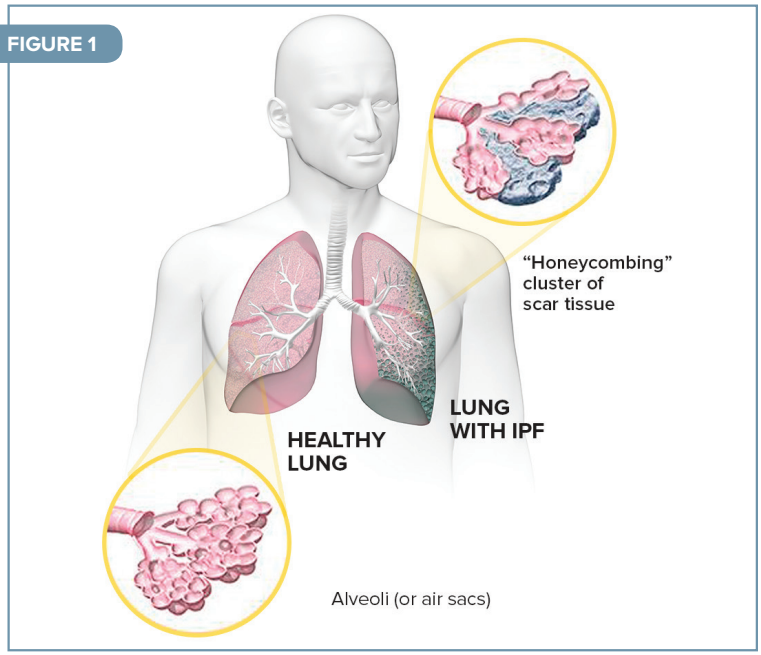
OFEV® is the first FDA-approved kinase inhibitor indicated for the treatment of idiopathic pulmonary fibrosis.[1]

OVERVIEW OF IDIOPATHIC PULMONARY FIBROSIS

Idiopathic pulmonary fibrosis (IPF) is a rare, chronic, progressive, lung disease with no definite known cause.[2] IPF affects up to 132,000 people in the United States,[3,4] and between 14,000 and 34,000 new IPF cases are diagnosed each year.[4] The disease mainly affects men,[2,4] smokers,[2] and people over the age of 50.[2,4]

IPF is the most frequent of the idiopathic interstitial pneumonias (IIPs), a group of diffuse parenchymal lung disorders characterized by varying patterns of fibrosis with no known etiology.[5] Arising spontaneously and without a clear origin, IPF causes scarring, architectural distortion, and permanent loss of function in lung tissue.[6] Imaging of affected lungs reveal key histopathological and/or radiological patterns associated with usual interstitial pneumonia (UIP), namely a reticular pattern of fibrosis with honeycombing (FIGURE 1). The fibrotic areas largely consist of dense collagen, but are also composed of fibroblasts and

FIGURE 1



IMPORTANT SAFETY INFORMATION[1]

WARNINGS AND PRECAUTIONS

Elevated Liver Enzymes

- OFEV is not recommended in patients with moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment.
- 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.

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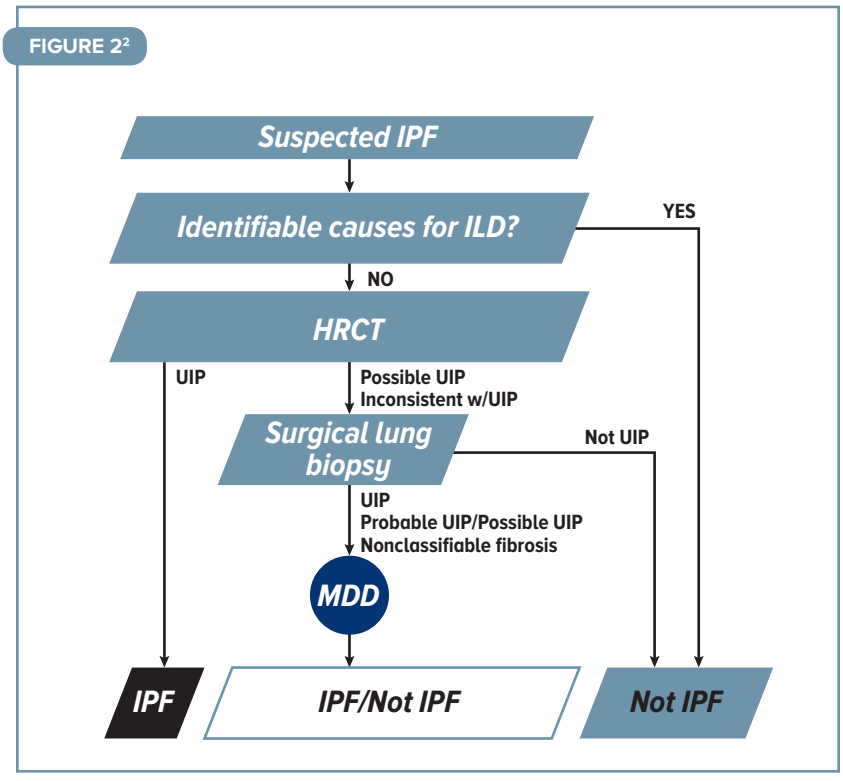
myofibroblasts.[7]

While the term UIP is often used interchangeably with IPF,[6] UIP often occurs in other interstitial lung diseases. Because the hallmark of IPF is that it is idiopathic—a disease or condition that presents suddenly without a known cause—it can only be diagnosed when other known causes of lung scarring or symptoms of pulmonary disease are excluded, including those caused by comorbidities such as connective tissue disease, certain medications, environmental and/or occupational exposures, and family history.[2] To help in making a positive diagnosis of IPF, the 2011 "Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis," a joint effort of ATS/ERS/JRS/ALAT, provided a diagnostic algorithm, which considers the role of HRTC in diagnosis.[2] (See adapted diagnostic algorithm FIGURE 2.)

FIGURE 2[2]



HRCT = high-resolution computed tomography; MDD = multidisciplinary discussion

While it is not yet known what initiates the pulmonary fibrosis brought on by IPF, it is thought that an abnormal "wound-healing" process occurring in the interstitial and alveolar spaces of the lung contributes to chronic pulmonary scarring.[8,9] Recent studies suggest that gastroesophageal reflux, environmental exposure, cigarette smoking, and/or viral infection, may be involved in the pathogenesis of the disease in susceptible individuals (genetics possibly playing a role).[2]

The triggering of cell-signaling pathways via tyrosine kinases—such as vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF)—have been implicated in the pathogenesis of IPF.[10] The recurrent and chronic damage of the alveolar epithelium, followed by an aberrant healing process characterized by unregulated proliferation of interstitial fibroblasts, is thought to give rise to IPF.[10]

Baseline pulmonary function tests—such as a forced vital capacity (FVC) test—is used as an established measure of monitoring disease progression for IPF. Limiting the annual rate of decline in FVC becomes vital in IPF care.

The rate of disease progression in IPF patients can occur gradually or more rapidly, and may be complicated by acute changes (acute IPF exacerbations).

IMPORTANT SAFETY INFORMATION[1]

WARNINGS AND PRECAUTIONS (cont'd)

Gastrointestinal Disorders

Diarrhea

- Diarrhea was the most frequent gastrointestinal event reported in 62% versus 18% of patients treated with OFEV and placebo, respectively. In most patients, the event was of mild to moderate intensity and occurred within the first 3 months of treatment. Diarrhea led to permanent dose reduction in 11% of patients treated with OFEV compared to 0 placebo-treated patients. Diarrhea led to discontinuation of OFEV in 5% of the patients compared to <1% of placebo-treated patients.
- Dosage modifications or treatment interruptions may be necessary in patients with adverse reactions of 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 despite symptomatic treatment, discontinue treatment with OFEV.

Please see additional Important Safety Information on the following pages and accompanying full Prescribing Information, including Patient Information.

OFFICIAL 2015 UPDATE TO THE 2011 IPF TREATMENT GUIDELINES[11]

The joint ATS/ERS/JRS/ALAT 2015 update to the 2011 "Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis" offers new recommendations for the treatment of IPF. Specifically, the Official Statement conditionally recommends the use of nintedanib, a triple kinase inhibitor, based on a moderate confidence in effect estimates.

When considering justification and implementation, the 2015 committee weighed the potential benefit, cost, and adverse effects for IPF patients. The committee placed "high value" on "patient-important outcomes." A "lower value" was placed on possible "significant adverse effects and the expected cost of treatment." The drug shows a "benefit in terms of patient-important outcomes" such as "disease progression as measured by rate of FVC decline." The committee's conditions on recommendations also took into account adverse effects and cost. Because adverse effects were commonly reported with therapy—most commonly diarrhea—patients should be informed of this when considering nintedanib. Moreover, "current costs [of nintedanib] may limit feasibility and use."

According to the methodology, "conditional recommendations" could be interpreted, for patients and clinicians, to mean that the majority of patients would want the suggested course of action, but many would not; and clinicians should recognize that different choices will be appropriate for individual patients and each patient must be helped to arrive at a management decision consistent with his or her values and preferences.

OFEV (nintedanib) CAPSULES AS A TREATMENT OPTION

Indications and Usage[1]

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

Description and Dosing[1]

OFEV capsules contain nintedanib, a kinase inhibitor. Nintedanib esylate is a bright yellow powder, distributed via 150 mg gelatin capsules (brown, opaque, oblong, and soft) and 100 mg gelatin capsules (peach, opaque, oblong, and soft).

Prior to initiating treatment, a liver function test should be conducted.

Recommended dosing is 300 mg a day, administered as 150 mg capsules taken orally twice daily, approximately 12 hours apart, taken with food and swallowed whole with liquid. The effect of chewing or crushing of the capsule on the pharmacokinetics of nintedanib is not known. If a dose of OFEV is missed, the next dose should be taken at the next scheduled time. Patients should be advised to not make up for a missed dose. Patients should not exceed the recommended maximum daily dosage of 300 mg.

Dosing modifications due to adverse reactions may be needed. In addition to symptomatic treatment, if applicable, the management of adverse reactions of OFEV may require dose reduction or temporary interruption until the specific adverse reaction resolves to levels that allow continuation of therapy. 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 a patient does not tolerate 100 mg twice daily, OFEV treatment should

Not shown at actual size

IMPORTANT SAFETY INFORMATION[1]

WARNINGS AND PRECAUTIONS (cont'd)

Gastrointestinal Disorders (cont'd)

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 is Pregnancy category D. It can cause fetal harm when administered to a pregnant woman and patients should be advised of the potential hazard to a fetus. Women should be advised to avoid becoming pregnant while receiving OFEV and to use adequate contraception during treatment and at least 3 months after the last dose of OFEV.

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be discontinued. Dose modifications or interruptions may be necessary for liver enzyme elevations. For aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >3 times to <5 times the upper limit of normal (ULN) without signs of severe liver damage, interrupt treatment or reduce OFEV to 100 mg twice daily. Once liver enzymes have returned to baseline values, treatment with OFEV may be reintroduced at a reduced dosage (100 mg twice daily), which subsequently may be increased to the full dosage (150 mg twice daily). Discontinue OFEV for AST or ALT elevations >5 times ULN or >3 times ULN with signs or symptoms of severe liver damage.

Clinical Pharmacology[1]

Mechanism of Action

Nintedanib is a small-molecule tyrosine kinase inhibitor, which inhibits vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF) and fibroblast growth factor (FGF) receptors—three receptors that have been implicated in IPF pathogenesis. Nintedanib binds competitively to the adenosine triphosphate (ATP) binding pocket of these receptors and blocks the intracellular signaling, which is crucial for the proliferation, migration, and transformation of fibroblasts representing essential mechanisms of the IPF pathology. OFEV is approved as the only kinase inhibitor indicated for the treatment of IPF by the FDA as of October 2014.[1]

Pharmacodynamics

Cardiac Electrophysiology

A single 200 mg oral dose of nintedanib, as well as multiple 200 mg doses of the drug administered twice daily for 15 days, did not prolong the QTcF interval in a study of renal cell cancer patients as QT/QTc measurements were recorded.

Pharmacokinetics

Clinical trials showed that the pharmacokinetic (PK) properties of nintedanib were similar in healthy volunteers, cancer patients, and patients with IPF. PK of nintedanib is linear, dose proportionality shown by an increase in drug exposure with increased dosing. Accumulation after several administrations in subjects with IPF was 1.76-fold for AUC. Steady-state plasma concentrations were attained within 1 week of dosing. Nintedanib trough concentrations remained steady for more than 1 year. The inter-individual variability in the PK of nintedanib was moderate to high, and intra-individual variability was low to moderate.

Maximum plasma concentrations are reached roughly 2 to 4 hours after oral administration under fed conditions. Nintedanib exposure increased by approximately 20% after food intake compared to administration under fasted conditions, and absorption was delayed.

Nintedinab follows bi-phasic disposition kinetics. After intravenous infusion, a high volume of distribution which was larger than total body volume (Vss: 1050 L) was observed. The *in vitro* protein binding of nintedanib in human plasma was shown to be high, with a bound fraction of 97.8%.

The effective half-life of OFEV in patients with IPF is roughly 9.5 hours, with approximately 0.05% urinary excretion of unchanged drug after oral dosing within 48 hours; the renal clearance is 20 mL/min. The prevalent metabolic reaction for nintedanib is hydrolytic cleavage by esterases resulting in the free acid moiety BIBF 1202. Only a minor extent of the biotransformation consisted of cytochrome P (CYP) pathways, with CYP3A4 being the predominant enzyme involved. The major CYP-dependent metabolite could not be detected in plasma in the human absorption, distribution, metabolism, and elimination study. Primary elimination of drug-related radioactivity after oral administration occurred through fecal/biliary excretion (93.4% of dose), and renal excretion to the total clearance is low (0.65% of the dose). Overall, elimination was considered complete (above 90%) within 4 days after dosing.

IMPORTANT SAFETY INFORMATION[1]

WARNINGS AND PRECAUTIONS (cont'd)

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.

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For specific populations, based on population PK analysis, age and body weight (but not sex) were associated with nintedanib exposure, but the effects were not great enough to merit a dose adjustment. The population PK analysis revealed that current smokers experience a 21% lower exposure of OFEV (nintedanib) capsules as compared to ex- and never-smokers; the effect is not great enough to merit a change in dosage.

PK analysis of data from 933 patients with IPF also showed that exposure to OFEV was not influence by mild (CrCI: 60 to 90 mL/min; n=399) or moderate (CrCI: 30 to 60 mL/min; n=116) renal impairment (CrCI below 30 mL/min); data of severe renal impairment was limited.

Efficacy of OFEV[1]

The efficacy of OFEV was evaluated in the phase 2 TOMORROW trial and in two replicate 52-week randomized, placebo-controlled phase 3 trials known as the INPULSIS® trials. In each trial, OFEV demonstrated reproducible and statistically significant reduction in the annual rate of FVC decline. In two out of three of these trials, data also revealed a significant reduction in the time to first acute IPF exacerbation, indicating that OFEV slows the overall disease progression of IPF.

OFEV as Treatment for IPF[1]

Clinical Studies

The clinical efficacy of OFEV has been studied in 1,231 patients with IPF in one phase 2 (TOMORROW; Study 1) and two phase 3 (INPULSIS®-1 and 2; Studies 2 and 3) trials. These were randomized, double-blind, placebo-controlled studies comparing treatment with OFEV 150 mg twice daily to placebo for 52 weeks.

Study 1 was similar in design to Studies 2 and 3, which were identical in design. Patients were randomized in a 3:2 ratio (1:1 for Study 1) to either OFEV 150 mg or placebo twice daily for 52 weeks. Study 1 also included other treatment arms (50 mg daily, 50 mg twice daily, and 100 mg twice daily) that are not further discussed. The primary endpoint was the annual rate of decline in FVC. Time to first acute IPF exacerbation was a key secondary endpoint in Studies 2 and 3 and a secondary endpoint in Study 1. Change from baseline in FVC percent predicted and survival were additional secondary endpoints in all studies.

Patients were required to have a diagnosis of IPF (ATS/ERS/JRS/ALAT criteria) for <5 years. Diagnoses were centrally adjudicated based on radiologic and, if applicable, histopathologic confirmation. Patients were required to be ≥40 years of age with an FVC ≥50% of predicted and a carbon monoxide diffusing capacity (DLCO, corrected for hemoglobin) 30% to 79% of predicted. Patients with relevant airways obstruction (i.e., pre-bronchodilator FEV_1/FVC <0.7) or, in the opinion of the investigator, likely to receive a lung transplant during the studies were excluded (being listed for lung transplant was acceptable for inclusion). Patients with >1.5 times ULN of ALT, AST, or bilirubin, patients with a known risk or predisposition to bleeding, patients receiving a full dose of anticoagulation treatment, and patients with a recent history of myocardial infarction or stroke were excluded from the studies. Patients were also excluded if they received other investigational therapy, azathioprine, cyclophosphamide, or cyclosporine A within 8 weeks of entry into this trial, or n-acetyl cysteine and prednisone (>15 mg/day or equivalent) within 2 weeks. The majority of patients were Caucasian (60%) or Asian (30%) and male (79%). Patients had a mean age of 67 years and a mean FVC percent predicted of 80%.

The primary endpoint for all three trials was the annual rate of decline in lung function as measured by FVC (FVC in mL). A statistically significant reduction in the annual rate of decline of FVC (in mL) was demonstrated in patients receiving OFEV (nintedanib) capsules compared to patients receiving placebo based on the random coefficient regression

IMPORTANT SAFETY INFORMATION[1]

WARNINGS AND PRECAUTIONS (cont'd)

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.

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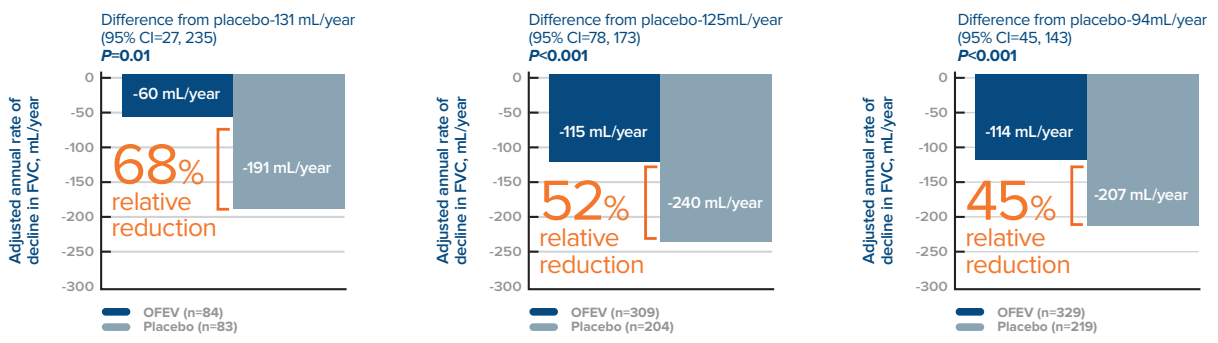
model, adjusted for gender, height, and age. All three trials demonstrated reproducible reduction in the annual rate of FVC decline for those patients administered OFEV (nintedanib) versus placebo; there was a 68%, 52%, and 45% relative reduction in the annual FVC decline in the TOMORROW, INPULSIS®-1, and INPULSIS®-2 trials, respectively. The difference in absolute values of annual rate of decline in FVC (mL) when comparing OFEV to placebo were statistically significant in all three trials: TOMORROW (131 [95% CI=27,235]), INPULSIS®-1 (125 [95% CI=78,173]), and INPULSIS®-2 (94 [95% CI=45,143]). Specifically, in the TOMORROW trial, a rate of decline over 52 weeks was -60 mL for patients being treated with OFEV, -191 for the placebo group; INPULSIS®-1: -115 (OFEV), -240 (placebo); and INPULSIS®-2: -114 (OFEV), -207 (placebo). The annual rate of decline in FVC, mL/year, for the TOMORROW, INPULSIS®-1 and INPULSIS®-2 trials can be seen in **FIGURE 3**.

Time to first acute IPF exacerbation was a key secondary endpoint in Studies 2 and 3 and a secondary endpoint in Study 1. Change from baseline in FVC percent predicted and survival were additional secondary endpoints in all studies.

Acute IPF exacerbation was defined as unexplained worsening or development of dyspnea within 30 days, new diffuse pulmonary infiltrates on chest x-ray, and/or new high-resolution CT parenchymal abnormalities with no pneumothorax or pleural effusion, and exclusion of alternative causes. Acute IPF exacerbation was adjudicated in Studies 2 and 3. In Studies 1 (investigator-reported) and 3 (adjudicated), the risk of first acute IPF exacerbation over 52 weeks was significantly reduced in patients receiving OFEV compared to placebo (hazard ratio [HR]: 0.16, 95% CI: 0.04, 0.71) and (HR:0.20, 95% CI: 0.07, 0.56), respectively. In Study 2 (adjudicated), there was no difference between the treatment groups (HR: 0.55, 95% CI: 0.20, 1.54).

Survival was evaluated for OFEV compared to placebo in Studies 2 and 3 in an exploratory analysis to support the primary endpoint (FVC). All-cause mortality was assessed over the study duration and available follow-up period, irrespective of cause of death and whether patients continued treatment. All-cause mortality did not show a statistically significant difference.

FIGURE 3[1]



IMPORTANT SAFETY INFORMATION[1]

DRUG INTERACTIONS

P-glycoprotein (P-gp) and CYP3A4 Inhibitors and Inducers

- Coadministration with oral doses of a Pgp 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.

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Safety and Adverse Event Data[1]

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of OFEV (nintedanib) capsules was evaluated in over 1,000 IPF patients with over 200 patients exposed to OFEV for more than 2 years in clinical trials. OFEV was studied in three randomized, double-blind, placebo-controlled, 52-week trials. In the phase 2 (Study 1) and phase 3 (Studies 2 and 3) trials, 723 patients with IPF received OFEV 150 mg twice daily and 508 patients received placebo. The median duration of exposure was 10 months for patients treated with OFEV and 11 months for patients treated with placebo. Subjects ranged in age from 42 to 89 years (median age of 67 years). Most patients were male (79%) and Caucasian (60%).

The most frequent serious adverse reactions reported in patients treated with OFEV, more than placebo, were bronchitis (1.2% vs. 0.8%) and myocardial infarction (1.5% vs. 0.4%). The most common adverse events leading to death in patients treated with OFEV, more than 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 treated patients and 1.8% of placebo-treated patients.

Adverse reactions leading to permanent dose reductions were reported in 16% of OFEV-treated patients and 1% of placebo-treated patients. The most frequent adverse reaction that led to permanent dose reduction in the patients treated with OFEV was diarrhea (11%).

Adverse reactions leading to discontinuation were reported in 21% of OFEV-treated patients and 15% of placebo-treated patients. The most frequent adverse reactions that led to discontinuation in OFEV-treated patients were diarrhea (5%), nausea (2%), and decreased appetite (2%).

The most common adverse reactions with an incidence of ≥5% and more frequent in the OFEV than placebo treatment group are listed in TABLE 1.

TABLE 1

ADVERSE EVENTS REPORTED IN ≥ 5% OF OFEV-TREATED PATIENTS AND MORE COMMONLY THAN IN PLACEBO[1]

	OFEV (n=723)	Placebo (n=508)
Diarrhea	62%	18%
Nausea	24%	7%
Abdominal pain	15%	6%
Vomiting	12%	3%
Liver enzyme elevations	14%	3%
Decreased appetite	11%	5%
Headache	8%	5%
Weight decreased	10%	3%
Hypertension	5%	4%

- In addition, hypothyroidism was reported in patients treated with OFEV (nintedanib) more than placebo (1.1% vs. 0.6%)[1]
- Liver enzyme increases were reversible with dose modification or interruption and not associated with clinical signs or symptoms of liver injury[1]

95% of diarrhea events — 95% of diarrhea events were mild or moderate in intensity[1,12,13]

First 3 months — The majority of diarrhea events occurred within the first 3 months of treatment[1]

5% of patients — 5% of all patients studied discontinued treatment due to diarrhea events[1,12]

IMPORTANT SAFETY INFORMATION[1]

USE IN SPECIFIC POPULATIONS

Nursing Mothers

- Excretion of nintedanib and/or its metabolites into human milk is probable. Because of the potential for serious adverse reactions in nursing infants from OFEV, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

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.

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PATIENT ASSISTANCE

Boehringer Ingleheim Pharmaceuticals, Inc., provides extensive assistance for IPF patients taking OFEV (nintedanib) capsules. The OPEN DOORS™ patient support network grants patients access to a support nurse, assistance in financial resources, access to information about IPF, and help identifying local resources. Patients also have access to a comprehensive treatment team to assist patients along their treatment journey. OFEV is only distributed through a specialty pharmacy and a list of partnering Special Pharmacies is available at *hcp.OFEV.com*.

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