OFEV®
nintedanib

Exploratory analysis suggests that OFEV® may extend life expectancy and is well tolerated in patients with IPF[1]

EXPLORATORY ANALYSIS BASED ON POOLED DATA FROM SIX INTERNATIONAL PHASE II/III OFEV® TRIALS INVESTIGATED:[1]

The extended safety and tolerability profile of OFEV®

The effect of OFEV® on survival in patients with IPF

INPULSIS® I and II[4] | TOMORROW[2,3] | Phase IIIb (double-blind)[6]

INPULSIS-ON® (open label)[5] | Phase IIIb (open label)

Pooled population	OFEV® 150 mg bid	Placebo
from 06 CLINICAL TRIALS	1126 PATIENTS	565 PATIENTS

1ST EXPLORATORY ANALYSES to estimate life expectancy in OFEV®-treated IPF patients[1]

LARGEST DATA SET ON OFEV® to be published to date[1] (based on extrapolation of survival data from clinical trials)

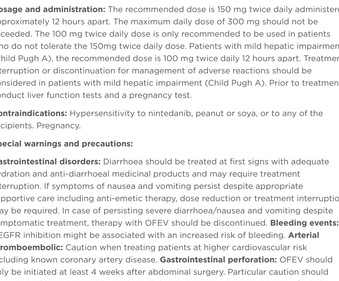
EXPLORATORY ANALYSIS SUGGESTS THAT OFEV® MAY EXTEND LIFE EXPECTANCY BY 5.2 YEARS IN PATIENTS WITH IPF[1]

Based on the Weibull distribution, mean (95% CI) survival was estimated as

11.6 YEARS (9.6, 14.10) in OFEV®-treated patients

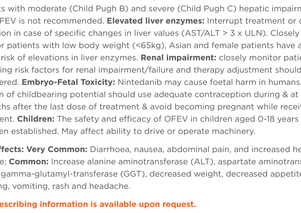
3.7 YEARS (2.5, 5.4) in placebo-treated patients

Estimated time to death



Adapted from Lancaster L, et al. *BMJ Open Resp Res.* 2019;6:e000397. doi:10.1136/bmjresp-2018-000397

Estimated median survival



Abbreviations

IPF, idiopathic pulmonary fibrosis; **BID**, twice daily

Weibull and exponential parametric survival distributions were fit to pooled Kaplan-meier survival data from the 6 trials. Model fit based on Akaike's information criterion was superior (lower) for the Weibull model compared with the exponential model in placebo-treated patients (428 vs 440) but not in the OFEV®-treated patients (1593 for both models.

References

1. Lancaster L, et al. *BMJ Open Resp Res.* 2019;6:e000397. doi:10.1136/bmjresp-2018-000397. **2.** Richeldi L, et al. *N Engl J Med.* 2011;365:1079-87. **3.** Richeldi L, et al. *Thorax.* 2018;73:581-3. **4.** Richeldi L, et al. *N Engl J Med.* 2014;370:2071-82. **5.** Crestani B, et al. *Lancet Respir Med.* 2019;7:60-8. **6.** Lancaster L, et al. Poster presented at: The Pulmonary Fibrosis Foundation 2017 Summit, 7-9 Nov 2017, Nashville, TN.

OFEV® Abbreviated Prescribing Information

Content: Nintedanib

Indications: OFEV is indicated in adults for the treatment of Idiopathic Pulmonary Fibrosis (IPF).

Dosage and administration: The recommended dose is 150 mg twice daily administered approximately 12 hours apart. The maximum daily dose of 300 mg should not be exceeded. The 100 mg twice daily dose is only recommended to be used in patients who do not tolerate the 150mg twice daily dose. Patients with mild hepatic impairment (Child Pugh A), the recommended dose is 100 mg twice daily 12 hours apart. Treatment interruption or discontinuation for management of adverse reactions should be considered in patients with mild hepatic impairment (Child Pugh A). Prior to treatment, conduct liver function tests and a pregnancy test.

Contraindications: Hypersensitivity to nintedanib, peanut or soya, or to any of the excipients. Pregnancy.

Special warnings and precautions:

Gastrointestinal disorders: Diarrhoea should be treated at first signs with adequate hydration and anti-diarrhoeal medicinal products and may require treatment interruption. If symptoms of nausea and vomiting persist despite appropriate supportive care including anti-emetic therapy, dose reduction or treatment interruption may be required. In case of persisting severe diarrhoea/nausea and vomiting despite symptomatic treatment, therapy with OFEV should be discontinued. **Bleeding events:** VEGFR inhibition might be associated with an increased risk of bleeding. **Arterial thromboembolic:** Caution when treating patients at higher cardiovascular risk including known coronary artery disease. **Gastrointestinal perforation:** OFEV should only be initiated at least 4 weeks after abdominal surgery. Particular caution should be exercised in patients with previous abdominal surgery, a recent history of a hollow organ perforation, previous history of peptic ulceration, diverticular disease or receiving concomitant corticosteroids or NSAIDs. **Soy lecithin:** Enhanced risk for severe reactions to soya preparations in patients with known allergy to peanut protein. **Hypertension:** Blood Pressure (BP) should be measured periodically. The use of VEGFR inhibitors may promote the formation of aneurysm and/or artery dissection, carefully considered in patients with poorly controlled hypertension or a history of aneurysm before treatment. **Hepatic impairment:** The safety, efficacy, and pharmacokinetics of nintedanib have not been studied in patients with severe renal impairment (<30 ml/min CrCL). Treatment of patients with moderate (Child Pugh B) and severe (Child Pugh C) hepatic impairment with OFEV is not recommended. **Elevated liver enzymes:** Interrupt treatment or dose reduction in case of specific changes in liver values (AST/ALT > 3 x ULN). Closely monitor patients with low body weight (<65kg), Asian and female patients have a higher risk of elevations in liver enzymes. **Renal impairment:** closely monitor patients exhibiting risk factors for renal impairment/failure and therapy adjustment should be considered. **Embryo-Fetal Toxicity:** Nintedanib may cause foetal harm in humans. Women of childbearing potential should use adequate contraception during & at least 3 months after the last dose of treatment & avoid becoming pregnant while receiving treatment. **Children:** The safety and efficacy of OFEV in children aged 0-18 years have not been established. May affect ability to drive or operate machinery.

Side effects: Very Common: Diarrhoea, nausea, abdominal pain, and increased hepatic enzyme; **Common:** Increase alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl-transferase (GGT), decreased weight, decreased appetite, bleeding, vomiting, rash and headache.

Full prescribing information is available upon request.

For Healthcare Professionals Only.

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