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Efficacy of Nintedanib for Idiopathic Pulmonary Fibrosis (IPF) and Its Safety for Breastfeeding and Pregnancy

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ABSTRACT

Background: An interstitial lung disease called pulmonary fibrosis can cause breathing difficulties by leaving scars in the lungs. Idiopathic Pulmonary Fibrosis (IPF) is the most prevalent kind of pulmonary fibrosis(PF). A multiple tyrosine kinase inhibitor called nintedanib received approval for use in antifibrotic treatment. There are two dosage forms for nintedanib: 100 mg and 150 mg for oral use. Two times a day, 150 mg should be taken with food. The Forced Vital Capacity (FVC) decrease was effectively reduced with nintedanib. In INPULSIS-1, INPULSIS-2, and a data set, the yearly rate of Forced Vital Capacity (FVC) decrease was considerably reduced in nintedanib users than in placebo users. The mortality rate from respiratory causes was 3.8% for patients who received nintedanib as opposed to 5.0% for patients who received a placebo. In this review, we mainly reviewed reports on the efficacy of nintedanib for Idiopathic Pulmonary Fibrosis (IPF) and its safety for breastfeeding and pregnant women. **Methods:** This review extracted the resources from PubMed by using the boolean method [" Efficacy of nintedanib" OR "nintedanib efficacy"] AND "pulmonary fibrosis". Compared to people who used a placebo in the INPULSIS-1 and INPULSIS-2 trials, nintedanib recipients showed significantly decreased annual rates of Forced Vital Capacity (FVC). Before beginning nintedanib and as needed throughout treatment, confirm your pregnancy status. Women should be informed that breastfeeding is not recommended due to the possibility of harmful side effects of nintedanib for nursing babies.
Conclusion: Patients treated with nintedanib observed a decreased rate of Interstitial Lung Disease development compared to those treated with placebo, but it's not recommended for pregnant and breastfeeding women.
Keyword: Efficacy, Nintedanib, Pulmonary Fibrosis

ABSTRAK

Latar Belakang: Penyakit paru interstisial yang disebut fibrosis paru dapat menyebabkan kesulitan bernapas dengan meninggalkan bekas luka di paru-paru. Fibrosis paru idiopatik merupakan jenis fibrosis paru yang paling banyak. Nintedanib merupakan inhibitor tirosin kinase yang digunakan dalam pengobatan antifibrotic. Ada dua bentuk sediaan nintedanib untuk dikonsumsi secara oral : 100 mg dan 150 mg. Dosis 150 mg dikonsumsi dua kali sehari bersama dengan makanan. Penggunaan nintedanib sangat efektif dalam penurunan Forced Vital Capacity(FVC) dalam INPULSIS-1, INPULSIS-2, dan kumpulan data, tingkat penurunan Forced Vital Capacity(FVC) tahunan sangat berkurang pada pengguna nintedanib daripada pengguna plasebo. Tingkat kematian akibat penyebab pernapasan adalah 3,8% untuk pasien yang menerima nintedanib dibandingkan dengan 5,0% untuk pasien yang menerima plasebo. Dalam ulasan ini, kami meninjau laporan tentang kemanjuran nintedanib untuk fibrosis paru idiopatik dan keamanannya untuk menyusui dan kehamilan. **Metode:** Ulasan ini mengambil sumber dari PubMed menggunakan metode boolean ["Efikasi nintedanib" ATAU "kemanjuran nintedanib"] DAN "fibrosis paru". Dibandingkan dengan orang yang menggunakan plasebo dalam uji coba INPULSIS-1 dan INPULSIS-2, penerima nintedanib menunjukkan tingkat Forced Vital Capacity (FVC) tahunan yang menurun secara signifikan. Sebelum memulai nintedanib dan sesuai kebutuhan

selama perawatan, konfirmasikan status kehamilan Anda. Wanita harus diberitahu bahwa menyusui tidak disarankan karena kemungkinan efek samping dari nintedanib yang berbahaya pada bayi menyusui.
Kesimpulan: Pasien yang diobati dengan nintedanib mengalami penurunan tingkat perkembangan penyakit paru interstitial dibandingkan yang diobati dengan plasebo dan tidak dianjurkan untuk wanita hamil dan menyusui.
Keyword: Efficacy, Nintedanib, Pulmonary Fibrosis

1. Introduction

Every year, over 50,000 new cases of Idiopathic Pulmonary Fibrosis (IPF) are identified. Idiopathic Pulmonary Fibrosis (IPF) mostly affects older male adults, typically between the ages of 50 and 70. Symptoms such as fatigue, dyspnea, and cough are common in older adults, which often results in insensitive detection and a delayed diagnosis. Clinical, radiologic, and histopathologic evaluations all contribute to the diagnosis.[1]

The prevalence rate of Idiopathic Pulmonary Fibrosis (IPF) is rising globally and is comparable to diseases like testicular, stomach, liver, and cervical cancer. Except for older research and populations from Asia and South America. Globally, the annual prevalence of Idiopathic Pulmonary Fibrosis(IPF) varies from 0.22 to 93.7 per 100,000 people; however, in North America in Europe, it is most likely to be between 2.8 and 9.3 per 100,000 people annually.[2] It is estimated that there are 200–500 instances of Idiopathic Pulmonary Fibrosis(IPF) for every 100,000 individuals.[3]

An interstitial lung disease called pulmonary fibrosis can cause breathing difficulties by leaving scars in the lungs. The reason for this is that scarring thickens and stiffens the lung tissues, which makes it more difficult for the blood to take oxygen. Idiopathic Pulmonary Fibrosis (IPF) is the most prevalent kind of Pulmonary Fibrosis (PF). The usual survival rate following diagnosis for Idiopathic Pulmonary Fibrosis (IPF), an age-related, persistent, progressive Interstitial Lung Disease (ILD) from uncertain etiology, is thought to be three to five years.[1]

Pulmonary function tests can be used to track the course of Idiopathic Pulmonary Fibrosis(IPF) disease. Two key indicators are Forced Vital Capacity (FVC) and the lung's ability to spread carbon monoxide. Long-term declines in the lung's ability to spread carbon monoxide and Forced Vital Capacity (FVC) have prognostic significance and are used to gauge how the disease is progressing.[1]

The receptors for platelet-derived growth factor, fibroblast, and vascular endothelial cells are the targets of nintedanib, a multiple tyrosine kinase inhibitor.[4] In 2014, nintedanib received approval for Idiopathic Pulmonary Fibrosis (IPF) in the US, and 2015 in Europe. Primarily targeting the receptor for platelet-derived growth factor (PDGFR), fibroblast growth factor (FGFR), and vascular endothelial growth factor (VEGFR), nintedanib also has pleiotropic effects on additional non-receptor tyrosine kinases.[5]

There are two dosage forms for nintedanib: 100 mg and 150 mg for oral use. Two times a day, 150 mg should be taken with food.[6]

The Forced Vital Capacity (FVC) decrease was effectively reduced with nintedanib. In INPULSIS-1, INPULSIS-2, and a data set, the yearly rate of Forced Vital Capacity (FVC) decrease was considerably reduced in nintedanib users than in placebo users. The incidence of a first acute exacerbation was considerably ($p < 0.05$) decreased by nintedanib compared to a placebo in a data set.[16]

This article discusses the safety and therapeutic efficacy that is still hampered by the lack of a sufficient preclinical model of Idiopathic Pulmonary Fibrosis (IPF), which is necessary to enhance research techniques for novel drugs. New drugs should be created taking into consideration the non-negligible incidence of comorbidities in Idiopathic Pulmonary Fibrosis (IPF) patients to guarantee that the trial results are widely relevant. In the end, they ought to be evaluated on a bigger sample of Idiopathic Pulmonary Fibrosis (IPF) patients and aim for a tolerable dosage. Ideally, forced vital capacity (FVC) should not be the only metric used to evaluate the effectiveness of possible nintedanib rivals.[7]

Before starting nintedanib, patients should have testing for liver function and a pregnancy test for potentially fertile females. Using nintedanib when pregnant may be harmful to the fetus. It is not recommended to use

nintedanib while pregnant in the EU or Canada. It is recommended that women in the United States who are capable of bearing children refrain from getting pregnant while on nintedanib.[8-10]

2. Method

This article is a descriptive study that explores the literature about the efficacy of nintedanib in IPF and its safety in breastfeeding and pregnancy between 2014-2024.

This review extracted the resources from PubMed. The boolean of literature searches is [" Efficacy of nintedanib" OR "nintedanib efficacy"] AND "pulmonary fibrosis". From those digital libraries gained 46 articles that explore nintedanib roles and efficacy in pulmonary fibrosis patients. Inclusion criteria for this research: literature review in 2014-2024, studies on animal, Idiopathic Pulmonary Fibrosis patients with pregnant and breastfeeding mothers, Idiopathic Pulmonary Fibrosis treatment with nintedanib. The exclusion criteria for this research: literature review other than 2014-2024, literature review other than English.

3. Result and Discussion

Result

For patients with Idiopathic Pulmonary Fibrosis (IPF), nintedanib remains a significant treatment option. The first medication authorized for use in other chronic fibrosing Interstitial Lung Disease (ILD) is nintedanib. The outcome of the INPULSIS trials demonstrated that nintedanib's impact on the possibility of investigator-reported acute exacerbations was variable. Some report that exacerbations are rare occurrences in patients with Idiopathic Pulmonary Fibrosis diagnosed on physical examinations. 26
With chest radiological examination and clinical examination, we were able to identify and enroll patients with a wide variety of fibrosing Interstitial Lung Diseases in the INBUILD trial. Compared to patients treated with a placebo, those treated with nintedanib experienced slower progression of Interstitial Lung Disease in both the entire population and patients with usual interstitial pneumonia (UIP)-like fibrotic type on high-resolution CT. The forced vital capacity showed a reduced yearly level of decline over 52 weeks to illustrate this. Patients with a Usual Interstitial Pneumonia (UIP) fibrotic type and those with other fibrotic types experienced comparatively lower levels of forced vital capacity decrease with nintedanib compared to placebo. 21

The INBUILD study not only investigated the effects of nintedanib but also offered valuable information about the record of increasing fibrosing Interstitial Lung Disease. Patients with usual interstitial pneumonia (UIP)-like fibrotic type and placebo-treated patients overall showed annual rates of decline in the forced vital capacity (FVC) that were comparable to those found in data from the INPULSIS trials for patients diagnosed with Idiopathic Pulmonary Fibrosis (IPF). According to earlier findings, patients receiving placebo treatment and having another type of fibrotic (non-UIP-like) experienced a decline in their FVC at a rate that was only marginally slower than that of patients with a UIP-like fibrotic type. This finding was significant. 27-29 In summary, patients treated with nintedanib observed a decreased rate of Interstitial Lung Disease development compared to those treated with placebo and it's not recommended for pregnant and breastfeeding women.

Discussion

Idiopathic Pulmonary Fibrosis (IPF) is defined as an abnormal growth in fibrotic tissue, which results in a gradual and irreversible decrease in lung function. Clinically, patients have decreasing lung volumes, a dry cough, and severe dyspnea. Even so, there is a lack of a precise estimate of the incidence and frequency of certain Interstitial Lung Diseases.[16]

The patient prognosis with Idiopathic Pulmonary Fibrosis (IPF) is three to five years following diagnosis.[16] The major goals of treating Idiopathic Pulmonary Fibrosis (IPF) are to reduce symptoms, and prevent acute exacerbations—which impact 5–15% of patients and can be fatal—slow the disease's development and increase survival time.[11,12] Patients must get preventive care, rehabilitation, and symptom-based treatment to stop their quality of life from declining.[13,14]

It is imperative to treat Idiopathic Pulmonary Fibrosis (IPF) early to improve clinical outcomes, minimize the possibility of acute exacerbations, and reduce the damage to lung function.[19] The tyrosine kinases of the receptors for a fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), and vascular endothelial growth factor (VEGF) are effective treatment targets in the management of Idiopathic Pulmonary Fibrosis (IPF). FGF, PDGF, and VEGF are known to mediate profibrotic processes and are connected to the etiology of IPF.[20]

In 2014, A multiple tyrosine kinase inhibitor called nintedanib received approval for Idiopathic Pulmonary Fibrosis (IPF) in the US, and in 2015, in Europe. Larger phase III (INPULSIS) studies were based on the positive outcomes of a phase II trial (TOMORROW) that examined nintedanib for IPF.[16]

To be eligible for the INPULSIS trials, which assessed the efficacy of nintedanib and its safety for IPF, A patient had to meet the following criteria: they had to be 40 years of age or older, have a forced expiratory volume in one second (FVC) of 0.7 or higher, a forced vital capacity (FVC) of 50% or higher, and a DLCO of 30 to 79% of the expected value. Similar to the TOMORROW project, the main outcome of the INPULSIS trial was the yearly rates of decrease in FVC.[16]

Table 1. Efficacy of Nintedanib for Idiopathic Pulmonary Fibrosis in Adults

Study	Adjusted annual rate of decline in FVC (mL/year)[a]	Adjusted mean change from BL in SGRQ total score [b]	≥ 1 Investigator-reported acute exacerbation (% of pts)[b]
INPULSIS-1			
Nintedanib (*n* = 309)	− 114.7	4.34	6.1
Placebo (*n* = 204)	− 239.9	4.39	5.4
Difference vs placebo (95% CI)	125.3 (77.7 to 172.8)**	− 0.05 (− 2.50 to – 2.40)	
Hazard ratio (95% CI)			1.15 (0.54 to 2.42)
INPULSIS-2			
Nintedanib (*n* = 329)	− 113.6	2.80	3.6
Placebo (*n* = 219)	− 207.3	5.48	9.6
Difference vs placebo (95% CI)	93.7 (44.8 to 142.7)**	− 2.69 (− 4.95 to – 0.43)*	
Hazard ratio (95% CI)			0.38 (0.19 to 0.77)*
INPULSIS-1 and -2 (prespecified pooled analyses)			
Nintedanib (*n* = *6*38)	− 113.6	3.53	4.9
Placebo (*n* = 432)	− 223.5	4.96	7.6
Difference vs placebo (95% CI)	109.9 (75.9 to 144.0)**	− 1.43 (− 3.09 to – 0.23)	
Hazard ratio (95% CI)			0.64 (0.39 to 1.05)

Notes: *BL* baseline, *FVC* forced vital capacity, *pts* patients, *SGRQ* St. George's Respiratory Questionnaire (range 0-100 points; higher scores indicate worse health-related quality of life)
*$p < 0.05$, **$p < 0.001$ vs placebo
[a] Primary endpoint for both INPULSIS trials (analysis included all available FVC values from BL to week 52, including measurements at follow-up visits for pts who prematurely discontinued the study drug; analysis allowed for missing data, assuming they were missing at random)
[b] Adjusted mean change from BL in SGRQ total score and time to first investigator-reported acute exacerbation were key secondary endpoints in both INPULSIS trials (assessed over a 52-week treatment period and evaluated hierarchically)

In INPULSIS-1, 513 patients received one dosage drug (309 patients accepted nintedanib and 204 accepted a placebo). 36 patients (17,6%) with placebo and 78 patients (25.2%) with nintedanib stopped taking the drug early. In INPULSIS-1, 31 (39.7%) with nintedanib and 11 (30.6%) with placebo finished their visits by 52 weeks. The most common cause for stopping to consume the drug was because of at least one adverse event (65 patients [21.0%] with nintedanib and 24 [11.8%] with placebo). In INPULSIS-2, 548 patients received one dose drug (329 with nintedanib and 219 with placebo). 78 patients (23.7%) with nintedanib and 44 patients (20.1%) with placebo stopped taking the drug early. In INPULSIS-2, 26 (33.3%) with nintedanib and 10 (22.7%) with placebo finished their visits by week 52.[16]

The forced vital capacity (FVC) decrease was effectively reduced with nintedanib. In INPULSIS-1, INPULSIS-2, and a data set, the yearly rate of Forced Vital Capacity (FVC) decrease was considerably reduced in nintedanib users than in placebo users ($p < 0.001$ versus placebo in each study). During 52-week, compared to placebo recipients, there was no absolute decrease in the percentage of predicted Forced Vital Capacity (FVC) of more than 5% (in both trials) or more than 10% (in INPULSIS-1 only), with a significantly ($p < 0.001$) higher proportion of nintedanib users; In the data set, in nintedanib users ($p < 0.001$), there was no significant decrease in Forced Vital Capacity (FVC) 5% (53% vs 39%) or of more than 10% (70% vs 61%) than placebo users.[16] According to the yearly rates of Forced Vital Capacity (FVC) change, 25% of patients

receiving nintedanib compared to 9% receiving placebo either showed an improvement in or no drop in Forced Vital Capacity (FVC).[19]

Nintedanib markedly extended the period of acute exacerbation in INPULSIS-2. (Table 1). However, Nintedanib showed significant benefit based on sensitivity analysis of the data set to the first confirmed or suspected acute exacerbation ($p = 0.001$) versus placebo. The incidence of a first acute exacerbation was considerably ($p < 0.05$) decreased by nintedanib compared to a placebo in a data set. Related to HR-QOL in INPULSIS-2, the total St. George's Respiratory Questionnaire (SGRQ) score of nintedanib is significantly improved from baseline to week 52 compared to placebo (Table 1). From baseline to 52 weeks, changes in St. George's Respiratory Questionnaire(SGRQ) domain score with total SGRQ score consistent.[16]

During the 52-week treatment duration, a predetermined data set revealed that the mortality rate with nintedanib was 5,5% and with placebo was 7,8% [hazard ratio (HR) 0.70; 95% confidence interval (CI) 0.43 to 1.12]. The mortality rate from respiratory causes was 3.8% for patients who received nintedanib as opposed to 5.0% for patients who received a placebo. 3.8% and 6.1% of patients who used nintedanib and placebo, accordingly, passed away within 28 days after the last dose.[16]

Phase III INBUILD trial was a double-blind, randomized, multinational, placebo-controlled research that assessed the efficacy of nintedanib for progressive fibrosing Interstitial Lung Disease. Adults with fibrosing interstitial lung disease diagnosed by a physician and who met the characteristics for progressive interstitial lung disease within the 24 months before diagnosis were eligible to participate in this trial. There are three possible outcomes for a relative Forced Vital Capacity (FVC) decrease : $\geq$ 10% of the predicted value, 5 to < 10% of the predicted value with worsening of respiratory symptoms on HRCT, or worsening respiratory symptoms with progressive fibrosis despite taking medication. Patients have at least 45% Forced Vital Capacity (FVC) of the expected value and 30% and <80% DLCO of the expected value.[21]

Patients can consume 150 mg of nintedanib for oral use two times a day (bid) or a placebo for 52 weeks, and the decrease of Forced Vital Capacity (FVC) in persons with Idiopathic Pulmonary Fibrosis was significantly decreased. The patient experiencing adverse effects (AE) was allowed to take 100 mg of nintedanib. Compared to placebo recipients in INPULSIS-1 and INPULSIS-2, nintedanib recipients showed significantly decreased annual rates of Forced Vital Capacity (FVC). [16]

In some studies of Usual Interstitial Pneumonia (UIP)-like fibrotic type or other fibrotic type, the development of fibrosing Interstitial Lung Disease in patients with Usual Interstitial Pneumonia (UIP) type on high-resolution CT faster than in those with other fibrotic type.[27-29] The experiment was divided into two parts: Part A, patients treated for the first 52 weeks, and Part B, Patients treated with nintedanib or placebo until all patients finished Part A after week 52. The main result was how decreased the annual value of Forced Vital Capacity (FVC) over a 52-week period. The main population for the experiment: general population and patients with Usual Interstitial Pneumonia (UIP)-like fibrotic type.[21]

Patients' mean age was 66 years, their Forced Vital Capacity (FVC) was 69% of the expected value, and their DLCO was 46% of the expected value in the overall population. Among the total population. Accordingly, 52 weeks of treatment were finished by 76% of nintedanib users and 85% of placebo users.[21]

In both the general population and patients with a Usual Interstitial Pneumonia (UIP)-like fibrotic type, nintedanib significantly ($p < 0.001$) decreased the yearly rate of Forced Vital Capacity (FVC) change in comparison to placebo (Table 2). The benefit of nintedanib over placebo for the yearly rate of Forced Vital Capacity (FVC) change (− 79.0 mL/year vs. − 154.2 mL/year; between-group difference 75.3 mL; 95% CI 15.5–135.0) was comparable to those observed in the general population in other fibrotic type.[21]

Decrease in Forced Vital Capacity (FVC) in nintedanib users based on Interstitial Lung Disease (ILD) diagnosis, age, sex, race, and baseline of FVC are largely consistent.[21-23] Decrease in annual value of Forced Vital Capacity (FVC) depending on treatment: 104.0 mL/year (95% CI 21.1-186.9) in autoimmune Interstitial Lung Disease, 73.1 mL/year (95% CI - 8.6 to 154.8) in hypersensitivity pneumonitis, 68.3 mL/year (95% CI – 31.4 to 168.1) in unclassifiable idiopathic interstitial pneumonia, 141.6 mL/year (95% CI 46.0–237.2) in idiopathic non-specific interstitial pneumonia, and 197.1 mL/year (95% CI 77.6–316.7) in other Interstitial Lung Diseases.[23]

On King's Brief Interstitial Lung Disease (K-BILD), the total score among nintedanib and placebo recipients had no significant change in the general population or the patients with Usual Interstitial Pneumonia (UIP)-like fibrotic type (Table 2). There was no significant change in the risk of acute exacerbations of Interstitial Lung Disease (ILD) or risk of death among nintedanib and placebo users during a 52-week treatment period.[21]

Table 2. The phase III INBUILD trial's findings on the efficacy of nintedanib for progressive fibrosing ILDs.

Primary population	Adjusted annual rate of decline in FVC (mL/year)[a]	Absolute change from BL in K-BILD total score at week 52[b]	Acute exacerbation of ILD or death at week 52 (% of pts)[b]	Death at week 52(% of pts)[b]
Overall population				
Nintedanib (*n* = 332)	− 80.8	0.55	7.8	4.8
Placebo (*n* = 331)	− 187.8	− 0.79	9.7	5.1
Difference vs placebo (95% CI)	107.0 (65.4 to 148.5) *	1.34 (−0.31 to 2.98)		
Hazard ratio (95% CI)			0.80 (0.48 to 1.34)	0.94 (0.47 to 1.86)
Pts with a UIP-like fibrotic pattern				
Nintedanib (*n* = 206)	− 82.9	0.75	8.3	5.3
Placebo (*n* = 206)	− 211.1	− 0.78	12.1	7.8
Difference vs placebo (95% CI)	128.2 (70.8 to 185.6)*	1.53 (−0.68 to 3.47)		
Hazard ratio (95% CI)			0.67(0.36 to 1.24)	0.68 (0.32 to 1.47)

Notes: *BL* baseline, *FVC* forced vital capacity, *ILD(s)* interstitial lung disease(s), *K-BILD* King's Brief Interstitial Lung Disease questionnaire (range 0-100 points; higher scores indicate better health status), *pt(s)* patient(s), *UIP* usual interstitial pneumonia.

*$p < 0.001$ vs placebo

[a] Primary endpoint (analysis based on all Forced Vital Capacity measurements over a 52-week period, including those from pts who prematurely discontinued the study drug; analysis allowed for missing data with the assumption they were missing at random)

[b] Absolute change from BL in K-BILD total score at week 52, time to first acute exacerbation of Interstitial Lung Disease or death over 52-week period were main secondary endpoints (not adjusted for multiple comparisons); pt numbers analyzed for K-BILD differ.

During all of the trial (mean exposure duration of 15.6 for nintedanib and 16.8 months for the placebo), 13.9% of nintedanib users and 19.6% of placebo recipients experienced an acute exacerbation of Interstitial Lung Disease or death (HR 0.67; 95% CI 0.46–0.98) in the general population, and 40.4% experienced disease progression (i.e., absolute decrease in Forced Vital Capacity ≥ 10% of the predicted value) versus 54.7% death (HR 0.66; 95% CI 0.53–0.83).[25]

Drug category D for pregnancy includes nintedanib. It should be used cautiously in women of reproductive age and stopped in nursing moms. Although nintedanib has not been studied in pregnant women, studies on animals have linked the drug to embryo-fetal mortality in rats and rabbits. Patients should be informed of the possible risks to a fetus when taking nintedanib because it can harm a developing fetus when given to a pregnant woman. When starting treatment, consuming the drug, and the last three months of the nintedanib dose, women should be told to avoid getting pregnant while on nintedanib and to use highly effective contraception.[18]

The information about the absorption of nintedanib in breast milk and the effects on babies who drink breast milk are unknown. For patients with SSc-ILD, nintedanib does not affect exposure to oral contraceptives that contain levonorgestrel and ethinylestradiol. However, diarrhea, vomiting, or other conditions that may reduce drug absorption may compromise the effectiveness of oral hormonal contraceptives. Encourage women using oral hormonal contraceptives and exhibiting these symptoms to switch to highly effective alternative forms of contraception. Before beginning nintedanib and as needed throughout treatment, confirm your pregnancy status. Women should be informed that breastfeeding is not advised due to the possibility of harmful side effects in nursing babies from nintedanib.[18]

4. Conclusion

Patients treated with nintedanib observed a decreased rate of Interstitial Lung Disease development compared to those treated with a placebo and it's not recommended for pregnant and breastfeeding women.

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