

Benefit and clinical characteristics after the use of Nintedanib in Idiopathic Pulmonary Fibrosis

Herrera-García José Carlos^a, Arellano Montellano Ek Ixel Ek Ixel^a, Jaramillo Arellano Luis

Enrique^b, Espinosa Arellano Andrea^b, Dr. José Carlos Herrera García^{c,*}

^a Department of Pulmonology. University Hospital of Puebla

^b Department of Undergraduate-Benemérita Autonomous University of the State of Puebla. ^c University Hospital of Puebla

1. SUMMARY

INTRODUCTION:

Nintedanib is an approved antifibrotic agent for the treatment of idiopathic pulmonary fibrosis. (FPI) as monotherapy. To date, the evidence supports its effectiveness in this type of patients.

METHODOLOGY

We present the case of a Mexican patient of 69 years with Idiopathic Pulmonary Fibrosis (IPF) treated with nintedanib for 52 weeks as monotherapy in a university hospital.

RESULTS:

Before the 52 week period. There was a clear decrease in the patient's forced vital capacity (FVC) from 70% (2.14L) to 60% (1.83L). The treatment with nintedanib was initiated for a period of 12 months at a dose of 150 mg VO every 12 hrs. Lung function stabilized increasing from 60% (1.83L) to 70% (2.14L), the treatment was well tolerated. Only with presence of mild adverse effects without repercussions.

CONCLUSIONS:

We describe the successful case of a patient with Idiopathic Pulmonary Fibrosis after 52 weeks of treatment with Nintedanib, well tolerated with improved lung function, until now the antifibrotic

therapy represents a safe and therapeutically option as monotherapy.

Introduction

Idiopathic pulmonary fibrosis (IPF) is a chronic and progressive lung disease characterized by a progressive worsening of lung function and an unfavorable prognosis. Recently, significant progress has been made in the treatment of this disease, and two different pleiotropic antifibrotic agents, pirfenidone and nintedanib, both received a conditional recommendation for use in patients with IPF based on the results of several multicenter studies demonstrating that they are effective to reduce lung damage. Both treatments are administered orally. (1)

In this case, we describe Nintedanib, an indolinone derivative, is a tyrosine kinase inhibitor that targets multiple tyrosine kinases, including the vascular endothelial growth factor receptor, the fibroblast growth factor receptor, and the receptor growth factor derived from platelets); it is known that these receptors are involved in the pathogenesis of IPF. It has been shown that Nintedanib inhibits the intracellular signaling pathways involved in proliferation, migration and differentiation of fibroblasts, and collagen synthesis and has demonstrated anti-inflammatory and anti-inflammatory activity in animal models of pulmonary fibrosis.(2-6)

Safety, tolerability and pharmacokinetics have been

previously evaluated in Japanese patients with IPF [16]. Gastrointestinal toxicity was the most common adverse effect and appeared to be more frequent with the treatment. Here, we report the case of a 69-year-old Mexican patient treated with nintedanib after the progression of the disease as a monotherapy. (7-9)

2. Report of a case

A 78-year-old man with no history of importance started with chronic cough, dyspnea mMRC 4, coughing in accesses and desaturation of 84%. Paraclinical studies and thorax tomography were performed, which showed data compatible with Idiopathic Pulmonary Fibrosis in January 2018. Start treatment with acetylcysteine, bronchodilators and oxygen.

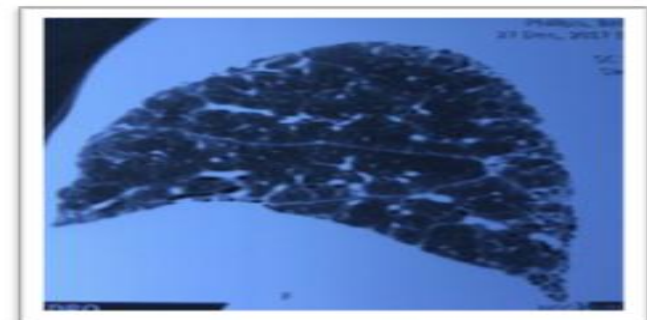
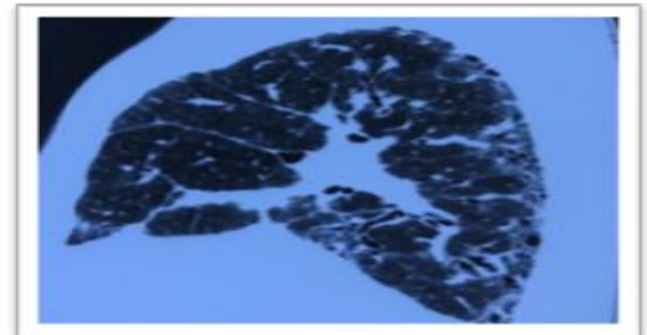
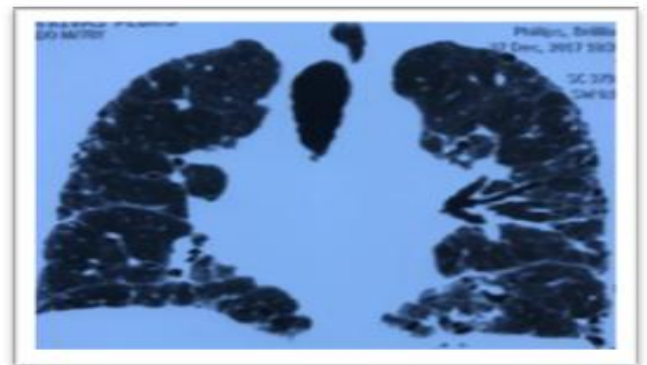
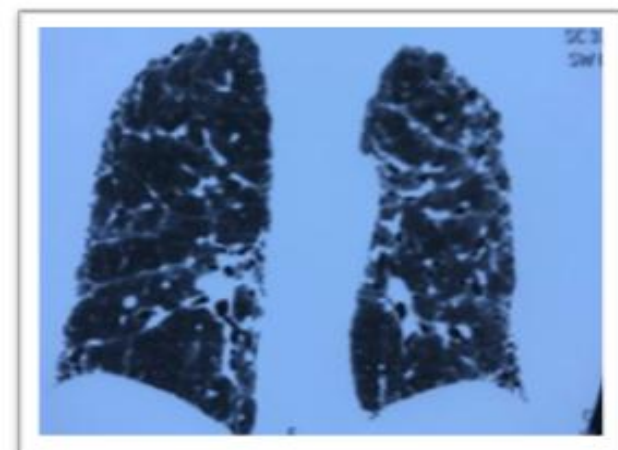
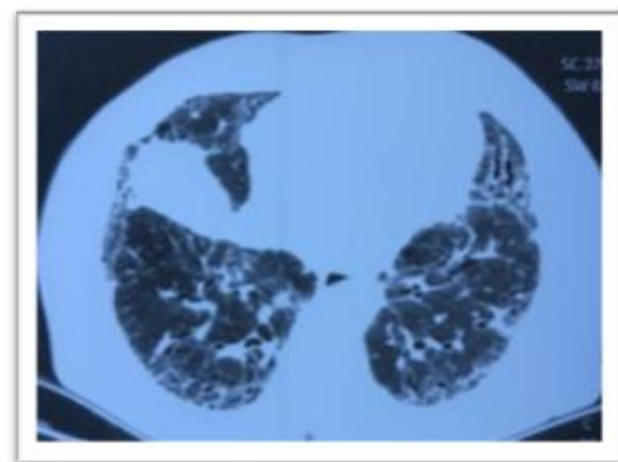
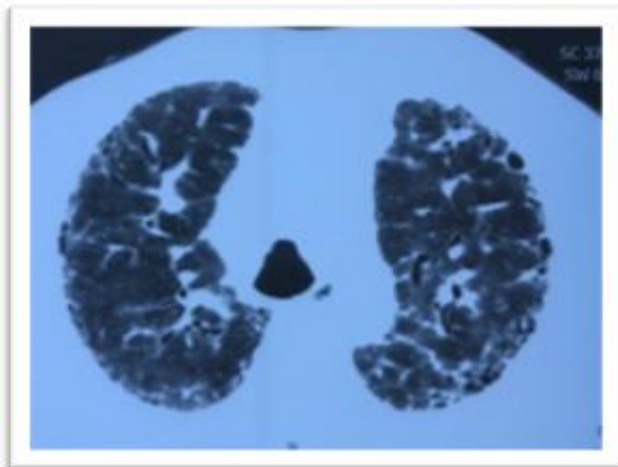


FIGURE 1.- Chest tomography with changes compatible with idiopathic pulmonary fibrosis.

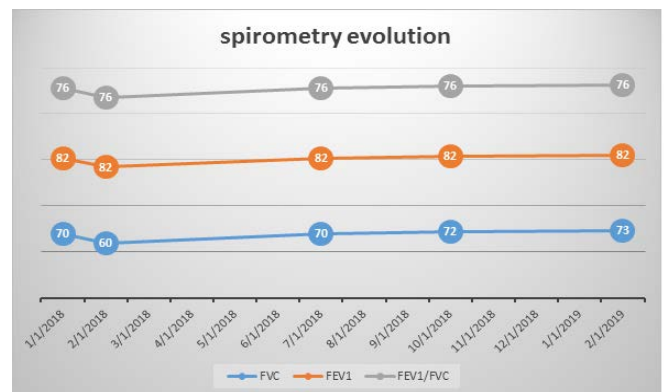


Figure 1 shows a high resolution computerized tomography at the time of diagnosis. During a period of 1 month, there was a clear decrease in the patient's forced vital capacity from 70% (2.14L) to 60% (1.83%) with 10% absolute reduction. After medical consensus, it was decided to start treatment with Nintedanib at a standard dose (150 mg every 12 hrs) for one month and it was well tolerated. In the second month it started with nausea, vomiting and dehydration that required hospitalization for 24 hrs with alteration of liver function tests (grade 3 toxicity). It was decided to continue the treatment with

Nintedanib at a dose of 100 mg every 12 hrs for 2 more weeks with good tolerance. After improvement of liver function tests, continue with a standard dose of 150 mg every 12 hours continuously, the treatment was well tolerated and compliance was good. In the fourth month, the patient stabilized the CVF from 60% (1.89L) to 70% (2.14L). The patient's body weight was 70 kg at the time of diagnosis, currently weighs 62 kg after 12 months of treatment, has not had new episodes of toxicity. Laboratory evaluations indicate that the patient has not experienced any abnormality in the hematological parameters. Therapy with nintedanib has been satisfactory for the patient, lung function and partial toxicity, no dose reductions or treatment interruptions of any of the medications have been necessary. Of importance to the patient, pulmonary function evaluations have demonstrated the stabilization of lung function as indicated by forced vital capacity that stabilized after 4 months. In February of 2019 he has completed 13 months of treatment with stable FVC in 73%. (2.23L)

3. DISCUSSION

The current treatment of idiopathic pulmonary fibrosis has been described as initial in patients with incipient disease and to prevent progression of the disease, in our case the patient initially presented a FVC according to age and weight, with continuous symptoms and progression rapid to the month of diagnosis, the new guidelines have allowed us to start treatment by a flow chart and tomographic by the severity of the disease without the need for biopsy, the patient's studies were approved by a committee of experts, because of this the patient could initiate treatment for the loss of 10% of CVF, so far it has only presented an occasional secondary adverse effects to the treatment already described and from there it has had a "tolerance" to the excellent treatment. This demonstrates the importance of an early diagnosis and timely treatment in patients with IPF.

4. CONCLUSION:

This paper describes the clinical characteristics of patients with IPF when receiving timely treatment with Nintedanib with adequate tolerance and stability of lung function tests. Giving the patient a better quality of life.

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5. BIBLIOGRAPHY

1. Ganesh Raghu, Martine Remy-Jardin, Jeffrey L. Myers, Luca Richeldi, Christopher J. Ryerson, David J. Lederer, Juergen Behr, Vincent Cottin, Sonye K. Danoff, Ferran Morell, Kevin R. Flaherty, Athol Wells, Fernando J. Martinez, Arata Azuma, Thomas J. Bice, Demosthenes Bouros, Kevin K. Brown, Harold R. Collard, Abhijit Duggal, Liam Galvin, Yoshikazu Inoue, R. Gisli Jenkins, Takeshi Johkoh, Ella A. Kazerooni, Masanori Kitaichi, Shandra L. Knight, George Mansour, Andrew G. Nicholson, Sudhakar N. J. Pipavath, Ivette Buendia-Roldan, Moises Selman, William D. Travis, Simon L. F. Walsh, and Kevin C. Wilson; on behalf of the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Society. Approved by the ATS, JRS and ALAT 2018 and the ERS June 2018. *Am J Respir Crit Care Med* 2018; 198:e44–e68.
2. Brunnemer et al. Real World Experience with Nintedanib in patients with Idiopathic Pulmonary Fibrosis: *Respiration* 2018; 1-9. DOI:10.1159/000485933.
3. Tabaj Gabriela et al: Experience with the compassionate use program of nintedanib for the treatment of idiopathic Pulmonary Fibrosis in Argentina: *RAMR: Volumen 17. No.2. Junio 2017*: 131-135.
4. Stefania Cerri et al: Occurrence of Idiopathic pulmonary Fibrosis during immunosuppressive treatment: a case report: *Journal of Medical Case Reports* 2016; 10:127. DOI 10.1186/s13256-016-0916-5.
5. Wollin L, Wex E, Pautsch A, Schnapp G, Hostettler KE, Stowasser S, Kolb M: Mode of action of nintedanib in the treatment of idiopathic pulmonary fibrosis. *Eur Respir J* 2015; 45: 1434–1445. Hagmeyer/Trembl/Priegnitz/Randerath *Respiration* 2016;91:327–332 DOI: 10.1159/000444690332
6. Antoniou KM, Symvoulakis EK, Anyfantakis D, Wells AU: New treatments for idiopathic pulmonary fibrosis: 'die another day' if diagnosed early? *Respiration* 2015; 90: 352.
7. Richeldi L, du Bois RM, Raghu G, Azuma A, Brown KK, Costabel U, Cottin V, Flaherty KR, Hansell DM, Inoue Y, Kim DS, Kolb M, Nicholson AG, Noble PW, Selman M, Taniguchi H, Brun M, Le Maulf F, Girard M, Stowasser S, Schlenker-Herweg R, Disse B, Collard HR, INPULSIS Trial Investigators: Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. *N Engl J Med* 2014; 370: 2071–2082.
8. Wollin L, Maillet I, Quesniaux V, Holweg A, Ryffel B: Antifibrotic and anti-inflammatory activity of the tyrosine kinase inhibitor nintedanib in experimental models of lung fibrosis. *J Pharmacol Exp Ther* 2014; 349: 209–220.
9. P, Piciocchi S, Dubini A, Carloni A, Chilosi M, Tomassetti S: Idiopathic pulmonary fibrosis: diagnosis and prognostic evaluation. *Respiration* 2013;86:5