Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

This clinical study synopsis is provided in line with **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country..

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's Policy on Transparency and Publication of Clinical Study Data**.

The synopsis is supplied for informational purposes only in the interests of scientific disclosure. It must not be used for any commercial purposes and must not be distributed, published, modified, reused, posted in any way, or used for any other purpose without the express written permission of Boehringer Ingelheim.

Proprietary confidential information © 2023 Boehringer Ingelheim International GmbH or one or more of its affiliated companies

SYNOPSIS

Company Name: Boehringer Ingelheim Korea			
Name of Finished Product: Ofev®			
Name of Active Ingredient: Nintedanib			
Date of Report: 18JAN2023	**Study No.:** 1199-0417	**Version/Revision:** 1.0	**Date of Version/Revision:** 06JAN2023
Title:	A Regulatory Required Non-Interventional Study to Monitor the Safety and Effectiveness of Ofev® (Nintedanib 150mg/100mg BID) in Korean Patients		
Keywords:	Ofev®, safety, efficacy, post-marketing surveillance, Korean		
Background:	As per the regulation, a non-interventional study (NIS) should be conducted upon approval of a new chemical entity (NCE). NIS can provide supplementary data to monitor the safety of NCE in a real world situation and additional data from clinical studies. Even if the safety information of Ofev® was confirmed in the clinical study setting, it can be administered to more diverse patients in a real world situation compared to patients limited to studies.		
Objective:	The study aims to monitor the safety profile and effectiveness of Ofev® in Korean patients in routine clinical settings.		
Methodology:	Non-interventional, multi-center study in Korea based on new collected data		
Setting:	Diagnosis • Patients diagnosed with idiopathic pulmonary fibrosis • (or) Patients diagnosed with systemic sclerosis associated interstitial lung disease • (or) Patients diagnosed with chronic fibrosing interstitial lung diseases with a progressive phenotype Inclusion Criteria: • Patients who have started on Ofev® in accordance with the approved label in Korea • Patients who have signed on the data release consent form Exclusion Criteria: • Patients for whom nintedanib is contraindicated according to local label of Ofev® I. Patients with known hypersensitivity to Ofev®, peanut or soya, or to any of the excipients II. Women who are pregnant or nursing III. Patients with moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment		

Proprietary confidential information © 2023 Boehringer Ingelheim International GmbH or one or more of its affiliated companies

Total Number of Subjects:	70 (safety assessment: 65, efficacy assessment: 20)
Endpoints and Sources:	Endpoints: Safety Endpoints All adverse events (AEs) that occurred in patients who received at least one dose of Ofev® were recorded. Efficacy Endpoints 1. Main Endpoint 1) Change from baseline in forced vital capacity (FVC, mL) at Weeks 12 and 24 after treatment 2. Other Endpoints 1) Change from baseline in FVC % predicted at Weeks 12 and 24 after treatment 2) Overall efficacy assessment result at Weeks 12 and 24 after treatment Data source: Study of sites collecting new data
Results:	During the re-examination period, the incidence of AEs reported in 65 subjects assessed for safety was 55.38% (36/65 subjects, 76 events). Among them, the incidences of adverse drug reactions (ADRs) for which the causal relationship to the drug cannot be ruled out, serious adverse events (SAEs), and serious adverse drug reactions (SADRs) were 36.92% (24/65 subjects, 40 events), 24.62% (16/65 subjects, 23 events), and 1.54% (1/65 subject, 1 event), respectively. The incidences of unexpected adverse events (UAEs) and unexpected adverse drug reactions (UADRs) were 36.92% (24/65 subjects, 38 events) and 12.31% (8/65 subjects, 8 events), respectively. The incidence of AEs leading to discontinuation of Ofev® was 12.31% (8/65 subjects, 13 events), and the incidence of AEs leading to reintroduction after discontinuation of Ofev® was 3.08% (2/65 subjects, 4 events). According to the post-marketing surveillance of Ofev®, no significant safety signal was observed. Among 20 subjects assessed for efficacy, the mean (SD) changes in FVC (mL) and FVC % predicted between before and after administration of the drug for 18 subjects assessed at Week 12 after administration were -15.00 (270.73) mL (*p*-value=0.8170) and 0.26 (6.28) % (*p*-value=0.8622), respectively, showing no statistically significant change, and the mean (SD) changes in FVC (mL) and FVC % predicted between before and after administration of the drug for 10 subjects assessed at Week 24 after administration were -44.00 (299.49) mL (*p*-value=0.6533) and -0.31 (7.10) % (*p*-value=0.8933), respectively, showing no statistically significant change.

Proprietary confidential information © 2023 Boehringer Ingelheim International GmbH or one or more of its affiliated companies

	According to the overall efficacy assessment result for 20 subjects included in the efficacy assessment, 30.00% (3/10 subjects) of 10 subjects assessed at Week 12 after administration were 'Improved', 60.00% (6/10 subjects) were 'Unchanged', and 10.00% (1/10 subject) was 'Aggravated', showing an effective rate of 30.00%, and according to the overall efficacy assessment result for 10 subjects assessed at Week 24 after administration, 40.00% (4/10 subjects) were 'Improved', 40.00% (4/10 subjects) were 'Unchanged', and 20.00% (2/10 subjects) were 'Aggravated', showing an efficacy rate of 40.00%. According to the efficacy assessment, the efficacy rate was lower than 50% because only 'Improved' was assessed as effective as per the protocol for post-marketing surveillance. However, patients with the indications for Ofev® have in general a relentless decline in lung function that can be more or less rapid. Therefore, 'Unchanged' is considered to demonstrate the efficacy of the drug. Given that this drug reduces the rate of FVC decline, some 'Aggravated' cases can also be considered to demonstrate the efficacy. Thus, the therapeutic effect of Ofev® in patients with idiopathic pulmonary fibrosis, chronic fibrosing interstitial lung diseases with a progressive phenotype, systemic sclerosis associated interstitial lung disease was assessed as effective.
Conclusion:	The safety information collected during this re-examination period was confirmed to be consistent with the local label, and its efficacy was favorable in general. Thus, the benefits are determined to outweigh the risks. Spontaneous reporting and relevant study results will continue to be collected in the future to identify factors affecting the safety and efficacy, and every effort will be made to manage the safety.
Marketing Authorization Holder:	Boehringer Ingelheim International GmbH
Name and Affiliation of Investigators:	Study site / Investigator [redacted]

Proprietary confidential information © 2023 Boehringer Ingelheim International GmbH or one or more of its affiliated companies