FIBRONET

STATISTICAL ANALYSIS PLAN

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Boehringer Ingelheim

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LIST OF ABBREVIATIONS

AE	Adverse Event
ALAT	Latin American Thoracic Association
ATS	American Thoracic Society
BAL	BronchoAlveolar Lavage
BITSPA	Boehringer Ingelheim Italy S.p.A.
BMI	Body Mass Index
BS	Biostatistician
CI	Confidence Interval
CDM	Clinical Data Manager
CNS	Central Nervous System
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
DLCO	Diffusion Lung Capacity for carbon monoxide
eCRF	Electronic Case Report Form
EQ-5D-5L	EuroQol 5-dimension 5-level
ERS	European Respiratory Society
FVC	Forced vital capacity
FEV1	Forced expiratory volume in the 1st second
HRCT	High Resolution chest Computer Tomography
HRQoL	Health Related Quality of Life
ILD	Interstitial Lung Disease
INHS	Italian National Health Service
IPF	Idiopathic Pulmonary Fibrosis
JRS	Japanese Respiratory Society
LTOT	Long-Term Oxygen Therapy
LTx	Lung Transplantation
Max	Maximum
MAH	Market Authorization Holder
MedDRA	Medical Dictionary for Drug Regulatory Activities
Min	Minimum
MMF	Mycophenolate MoFetil
N	Number of observations
NIS	Non-interventional Study
p.o.	per os (oral)
PRO	Patient Related Outcomes
q.d.	quaque die (once a day)
QoL	Quality of Life
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
s.c.	subcutaneous
SGRQ	St. George's Hospital Respiratory Questionnaire
SD	Standard Deviation
t.i.d.	ter in die (3 times a day)
VC	Vital Capacity
TLC	Total Lung Capacity
UIP	Usual Interstitial Pneumonia

1 STATISTICAL ANALYSIS PLAN OBJECTIVES

The FIBRONET study is a multi-center, non-interventional (observational) prospective cohort study based mainly on newly collected data. A total of 200 consecutive patients will be enrolled in approximately 18 months (from the first patient enrolled). Patients will be followed-up for 1 year, with 3 intermediate evaluations after 3 (±1), 6 (±1) and 9 (±1) months since baseline (which is compatible with current clinical practice in Italy for IPF patients management).
The present Statistical Analysis Plan has beed designed considering the following input documents: the Study Protocol v.1.0 26/06/2015 and the electronic case report form v. 1.1.1 30/11/2015.
This SAP is aimed at evaluating the following study objectives:

Primary objective:

1. In a sample of IPF diagnosed patients to describe the clinical course during 12 months of observation, in terms of:
   - IPF symptoms
   - lung function (VC, FVC, FEV1, TLC, DLCO, pO2, pCO2; SaO2, PaO2 and PaCO2 at rest)
   - exercise tolerance (6-minute walk distance test)

Secondary objectives:

1. Description of characteristics of IPF patients at enrollment in terms of:
   - key (socio-) demographic data
   - IPF risk factors, comorbidities
   - IPF disease severity and manifestation (including lung function, cardiopulmonary exercise testing and/or exercise capacity if available, laboratory values)
   - Methods used for IPF diagnosis
   - IPF treatment modalities (detailed information on prescribed drugs and dose; non-pharmacological treatment; lung transplantation)
2. To describe the frequency of exacerbations during 12 months of observation.
3. To describe HRQoL variation, measured with SGRQ, EuroQol (EQ) 5-dimension 5-level (EQ-5D-5L) descriptive system and EQ VAS, during 12 months of observation.
4. To describe health care sector-related costs from diagnosis up to the end of 12-month follow-up according to the Italian National Health Service (INHS) point of view.

The ongoing (pharmacological and non-pharmacological) therapies at each follow up will be described too.

In this document the eCRF fields are indicated as follows: “label of the field” [***name of the eCRF form.name of the variable in the dataset***].

2 DEFINITION OF EVALUABLE PATIENTS

All enrolled patients fullfilling the following criteria will be considered evaluable for the evaluation of FIBRONET primary study objective:

2.1 Patients evaluable at enrollment[1]

All enrolled patients meeting the following inclusion and exclusion criteria will be considered evaluable at enrollment:

1. Patient aged>=40 years

- *Question "1. Patient aged>=40 years" = "Yes"* ***[F01_INC_EXC_CRITERIA.CI_1]***
  AND
- *Age at enrollment visit (years) ≥ 40* ***[_PatientInfo.Age]***
  AND
  1. Patients aged >= 40 years ***[F27_PROTOCOL_DEVIATION_FORM.PD_CI_1]*** *not checked*

2. Written informed consent to both participation in the study and privacy

- *Question "2. Written informed consent to both participation in the study and privacy" = "Yes"* ***[F01_INC_EXC_CRITERIA.CI_2]***
  AND
- *Date of informed consent signature (dd/mm/yyyy) not missing* ***[_PatientInfo.Date_CI]***
  AND
- *Date of privacy form signature (dd/mm/yyyy) not missing* ***[_PatientInfo.Date_privacy]***
  AND
  Date of privacy form signature (dd/mm/yyyy) ≤ Date of enrollment visit (dd/mm/yyyy)
  AND
  Date of informed consent signature (dd/mm/yyyy) ≤ Date of enrollment visit (dd/mm/yyyy)
  AND
  2. Written informed consent to both participation in the study and privacy ***[F27_PROTOCOL_DEVIATION_FORM.PD_CI_2]*** *not checked*

3. Physician diagnosed IPF during the last 3 months based upon recent ATS/ERS/JRS/ALAT guidelines 2011 (see Tables A1-A2 of study protocol - Annex 1):

- *- Exclusion of other known causes of ILD (e.g. domestic and occupational environmental exposures, connective tissue disease and drug toxicity)*
  - Assessment of IPF based on HRCT or HRCT and surgical lung biopsy if available.*

  Question "3. Physician diagnosed IPF during the last 3 months based upon recent ATS/ERS/JRS/ALAT guidelines 2011*" = "Yes"* ***[F01_INC_EXC_CRITERIA.CI_3]***
  AND
- *Date of first IPF diagnosis (mm/yyyy) not missing or NK* ***[F05_DIAGNOSIS_IPF.Dia_Date_IPF_Diagnosis]***
  AND
- *round ((Date_enrollment* - Date of first IPF diagnosis)/30.4375) ≤ 3*
  AND
- *Date of first IPF diagnosis (mm/yyyy) ≤ Date of enrollment visit (dd/mm/yyyy)*
  AND
- *IPF diagnosis based on* ***[F05_DIAGNOSIS_IPF.Dia_IPF_diagnosis_based_on, DIA_IPF_based_on_other]*** *must include the following options: "HRCT" or ("HRCT" and "Surgical lung biopsy").*
  AND
- *3. Physician diagnosed IPF during the last 3 months based upon recent ATS/ERS/JRS/ALAT guidelines 2011 (see Tables A1-A2 for HRCT and histology criteria)* ***[F27_PROTOCOL_DEVIATION_FORM.PD_CI_3]*** *not checked*

  In case of missing month or day in date of first IPF diagnosis they will be considered respectively =01 and =July.

  **It will be recalculated considering for all patients day=01.*

[1] The number of patients evaluable for analyses will be previously shared with sponsor for approval before first release of statistical report.

4. Patient with further follow-up possible with enrolling investigator during planned study period

- *Question "4. Patient with further follow-up possible with enrolling investigator during planned study period" = "Yes" **[F01_INC_EXC_CRITERIA.CI_4]***
  AND
- *4. Patient with further follow-up possible with enrolling investigator during planned study period **[F27_PROTOCOL_DEVIATION_FORM.PD_CI_4]** not checked*

5. Patient capable of discernment and able to read or write in Italian language

- *Question "5. Patient capable of discernment and able to read or write in Italian language" = "Yes" **[F01_INC_EXC_CRITERIA.CI_5]***
  AND
- *5. Patients capable of discernment and able to read or write in Italian language. **[F27_PROTOCOL_DEVIATION_FORM.PD_CI_5]** not checked*

6. Patient not included in clinical trials or other IPF/ILD registries

- *Question "6. Inclusion in clinical trials or other IPF/ILD registries" = "No" **[F01_INC_EXC_CRITERIA.EC_1]***
  AND
- *1. Inclusion in clinical trials or other IPF/ILD registries **[F27_PROTOCOL_DEVIATION_FORM. PD_EC_1]** not checked*

7. Patient without lung transplantation expected within the next 6 months

- *Question "7. Lung transplantation expected within the next 6 months " = "No" **[F01_INC_EXC_CRITERIA.EC_2]***
  AND
- *2. Lung transplantation expected within the next 6 months **[F27_PROTOCOL_DEVIATION_FORM. PD_EC_2]** not checked*

8. Female patient not pregnant at enrollment or breast feeding

- *Question "8. Pregnancy or breast feeding" = "No" **[F01_INC_EXC_CRITERIA.EC_3]***
  AND
- *3. Pregnancy or breast feeding **[F27_PROTOCOL_DEVIATION_FORM. PD_EC_3]** not checked*

9. Male and female patients

- *Gender at enrollment visit **[_PatientInfo.Gender]** not missing*

10. Available evaluation of at least one of the following at enrollment:
    - IPF symptoms
      - *IPF symptoms at study visit? **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms_YN]**= Yes and at least one symptom **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms, SYM_IPF_symptoms_other]** not missing OR IPF symptoms at study visit?= No OR mMRC dyspnea score **[F15_MMRC.MMRC]** not missing.*
    - Lung function (VC, FVC, FEV1, TLC, DLCO, pO2, pCO2; SaO2, PaO2 and PaCO2 at rest)
      - [**F07_LUNG_FUNCTION_ASS. LU_Spirometry_YN**]=*Yes and at least one parameter* [**F07_LUNG_FUNCTION_ASS. LU_FEV1-- LU_saO2_Num**] *not missing.*
      - [**F07_LUNG_FUNCTION_ASS. LU_Emogas_YN]**=*Yes and at least one parameter* [**F07_LUNG_FUNCTION_ASS. LU_PO2_Num, LU_PaO2_Num, LU_PCO2_Num, LU_PaCO2_Num**] *not missing.*
    - Exercise tolerance (6-minute walk distance test)
      - [**F07_LUNG_FUNCTION_ASS. LU_6_Minute_YN]**=*Yes and 6-minute walked distance (m)* [**F07_LUNG_FUNCTION_ASS. LU_6_minute_distance_Num]** *not missing.*

3 COMPUTED VARIABLES

The following variables will be computed as described below.

BMI

BMI index will be computed as follows: Weight (Kg) **[F02_SOCIO_DEMOGRAPHICS.SD_Weight_Num]**/(Height (cm) **[F02_SOCIO_DEMOGRAPHICS.SD_Height_Num]** *100) ^ 2

Underweight: BMI < 18.5, normal weight: BMI 18.5-24.9, overweight: BMI 25-29.9, obese: BMI >= 30.

Smoking duration at enrolment (years)

- For patient who are current smokers by the time of enrolment ([**F03_IPF_RISK_FACTORS.RF_smoking**] = "Current smoker"): Smoking duration at enrolment = YEAR (Date of enrolment visit [**_PatientInfo.Date_enrollment**]) – Start year [**F03_IPF_RISK_FACTORS.RF_start_year**]), if Start year and Date of enrolment visit are not missing.
- For patient who are former smokers by the time of enrolment ([**F03_IPF_RISK_FACTORS.RF_smoking**] = "Former smoker"): Smoking duration at enrolment = Stop year [**F03_IPF_RISK_FACTORS.RF_stop_year**] – Start year [**F03_IPF_RISK_FACTORS.RF_Start_year**]), if Stop year and Start year are not missing.

Comorbidities at enrollment

The comorbidities in class other **[F04_COMORBIDITIES.COM_Comorbidities_other]** will be translated into English and typos will be corrected. Moreover, CDM will recod them into the classes of field Comorbidity **[F04_COMORBIDITIES.COM_Comorbidities]** (Atherothrombotic disease including coronary heart disease, Cerebrovascular disease, etc..), if necessary.

The patients with Comorbidity **[F04_COMORBIDITIES.COM_Comorbidities]**=Other and **[F04_COMORBIDITIES.COM_Comorbidities_other]** = BENIGN PROSTATIC HYPERTROPHY or HYPERCHOLESTEROLEMIA will be considered with Comorbidity **[F04_COMORBIDITIES.COM_Comorbidities]**= Benign Prostatic Hypertrophy or Hypercholesterolemia.

Methods of diagnosis (other)

The following self-evident corrections will be applied:

- If IPF diagnosis based on other test, specify **[F05_DIAGNOSIS_IPF.DIA_IPF_based_on_other]** ="CT with cotrast medium on Ago 2015 (no UIP); PET in Sep 2015 (possible Interstitial disease)" then DIA_IPF_diagnosis_based_on_other ="CT;PET";
- if DIA_IPF_diagnosis_based_on_other = 'crio biopsy', 'crio-biopsy', 'criobiopsy', 'cryobiopsy', 'cryobiospy' then DIA_IPF_diagnosis_based_on_other ="CRYOBIOPSY";
- if DIA_IPF_diagnosis_based_on_other ='Bioumoral examination for autoimmunity exclusion' or 'biopsy salivary gland for autoimmunity exclusion' then DIA_IPF_diagnosis_based_on_other ='TEST FOR AUTOIMMUNITY EXCLUSION'.

Patient who performed V2 (3-months), V3 (6-months), V4 (9-months), V5 (12-months) follow up visit

At each follow up visit they will be defined as patients satisfying the following criteria:

1. Patients evaluable at enrollment (i.e., responding to criteria of par 2.1 Patients evaluable at enrollment)

2. Data collected at x-month follow-up = "Yes" **[F16_PATIENT_DISPOSITION, 3 month f-up.PD_1; 6 month f-up.PD_1; 9 month f-up.PD_1; 12 month f-up.PD_1]**
where x=3-, 6-, 9-, 12-

3. Follow-up performed at x ±1.5 months from enrollment *(where x=3-, 6-, 9-, 12-)*

- *(Date of follow up visit (dd/mmm/yyyy)* **[F16_PATIENT_DISPOSITION, 3 month f-up.PD_2; 6 month f-up.PD_2; 9 month f-up.PD_2; 12 month f-up.PD_2]***– Date of enrolment visit (dd/mm/yyyy)* **[_PatientInfo. Date_enrollment]***/30.4375 ≥ 1.5 (or 4.5 or 7.5 or 10.5))*
AND
- *(Date of follow up visit (dd/mmm/yyyy)* **[F16_PATIENT_DISPOSITION, 3 month f-up.PD_2]***– Date of enrolment visit (dd/mm/yyyy)* **[_PatientInfo. Date_enrollment]***/30.4375 ≤ 4.5 (or 7.5 or 10.5 or 13.5))*

4. With available IPF symptoms evaluation at baseline and at x ±1.5 months from enrollment *(where x=3-, 6-, 9-, 12-)*

- *(IPF symptoms at baseline ?* **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms_YN]***=No OR (IPF symptoms at baseline?=Yes AND at least one symptom* **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms, SYM_IPF_symptoms_other]** *not missing))*
AND
- (IPF symptoms at x-month follow up? **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms_YN]**=No OR *(IPF symptoms at x-month follow up?=Yes AND at least one symptom* **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms, SYM_IPF_symptoms_other]** *not missing)*
where x=3-, 6-, 9-, 12-

IPF symptoms
For patients with *if other symptom, specify* **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms, SYM_IPF_symptoms_other]** =EXERTIONAL DYSPNEA or DISABLING DYSPNEA the field will be considered as DYSPNEA.

Incident IPF symptom at x-month follow up
IPF symptom absent at enrollment visit and present at x-month follow-up visit) **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms]**
Where x=3-, 6-, 9-, 12-

Patients with incident IPF symptom at x-month follow up
Patients with incident IPF symptom (according to previous definition) over total number of patients without symptom at baseline.
Where x=3-, 6-, 9-, 12-

Remitted IPF symptom at x-month follow up
IPF symptom present at enrollment visit and absent at x-month follow-up visit) **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms]**
Where x=3-, 6-, 9-, 12-

Patients with remitted IPF symptom at x-month follow up
Patients with remitted IPF symptom (according to previous definition) over total number of patients with symptom at baseline.
Where x=3-, 6-, 9-, 12-

Lung function assessment

For a patient with FEV1 (L)=170 at baseline and for a patient with FVC (L)=1330 at 3-month follow up the values will be set to missing.
Values of DLCO with unit **[F07_LUNG_FUNCTION_ASS.LU_DLCO_unit]**=ml/min/mmHg will be converted to mmol/min/kPa according to the following formula: DLCO (mmol/min/kPa)=DLCO (ml/min/mmHg)/2.986 (*reference: Diffusing Capacity: How to get it right Jensen R and Crapo RO Respir Care 2003: 48 (8): 777-782*).

At each follow up visits the absolute changes of lung function assessments vs baseline values will be calculated as:
Change $_{\text{parameter x}}$= value of parameter x at follow up i visit - value of parameter x at baseline visit.
Where x= FEV1, FEV1 of the predicted, FVC, FVC of the predicted, FEV1/FVC, VCin, RV, TLC, DLCO, DLCO of the predicted, SaO2 and all parameters of emogas analysis and i= follow up at 3, 6, 9, 12 months.

The relative change of FVC of the predicted (%) will be calculated as:
Change $_{\text{FVC of the predicted (\%)}}$= (value of FVC of the predicted (%) at follow up i visit -value of FVC of the predicted (%) at baseline visit)/ value of FVC of the predicted (%) at baseline visit*100.
Where i= follow up at 3, 6, 9, 12 months.
The following classes will be considered for the relative change of FVC of the predicted (as described above) between baseline and follow up: <5%; 5-10%; >10%.

Patient with at least one exacerbation since IPF diagnosis till end of observation period

The proportion of patients with at least one exacerbation during observation period will be computed as the ratio between the number of patients with one or more episodes of exacerbation occurred since IPF diagnosis till end of observation period over the total number of evaluable patients. Patients who drop-out without having exacerbations before the end of the study, will be considered in the denominator of the proportion of interest.
An exacerbation will be considered occurred during observation period if onset date **[F08_EXACERBATIONS.Ex_Exacer_1_Ons_date-Ex_Exacer_10_Ons_date]** >=date of first IPF diagnosis (mm/yyyy) **[F05_DIAGNOSIS_IPF.DIA_Date_IPF_diagnosis]** and onset date **[F08_EXACERBATIONS.Ex_Exacer_1_Ons_date-Ex_Exacer_10_Ons_date]** <= last available visit date **[P16_PATIENT_DISPOSITION.PD_2]** (for patients who completed the study **[F19_STUDY_COMPLETION.SC_1]** = Yes) OR date of Date of drop out or death **[F19_STUDY_COMPLETION.SC_4, SC_5]** (for patients who did not complete the study **[F19_STUDY_COMPLETION.SC_1]** = No).

Health Related Quality of Life (HRQoL) EQ-5D-5L (see Appendix 8.3)

The EQ-5D-5L is a standardized measure of health status, it is filled in by patients. It consists of 2 sections: "EQ-5D descriptive system" and EQ visual analogue scale (EQ VAS).

[2] *Perez T. et al. Modified Medical Research Council scale vs Baseline Dyspnea Index to evaluate dyspnea in chronic obstructive pulmonary disease Int J Chron Obstruct Pulmon Dis. 2015; 10: 1663–1672.*

The EQ-5D-5L descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.
The EQ VAS indicate the health status self-assessed by the patient on a visual analogue scale from 0 to 100, where 100 is the "best imaginable health state" and 0 the "worst imaginable health state". It can be used as a quantitative measure of health as judged by respondents.

St. George's Respiratory Questionnaire (SGRQ) (see Appendix 8.5)
The SGRQ is designed to measure health impairment in patients with asthma and COPD.
There is a report of its validation in a small study of adults with cystic fibrosis (Archivos de Bronconeumologia Volume 43, Issue 4, April 2007, pages 205-211). It is in two parts. Part I produces the Symptoms score, and Part 2 the Activity and Impacts scores. A Total score is also produced.
Part 1 (Questions 1-8) addresses the frequency of respiratory symptoms. It is not designed to be a precise epidemiological tool, but to assess the patient's perception of their recent respiratory problems.
Part 2 (Sections 9-17) addresses the patient's current state (i.e. how they are these days).

The Activity score measures disturbances to daily physical activity. The Impacts score covers a range of disturbances of psycho-social function. Validation studies for the original SGRQ showed that this component relates in part to respiratory symptoms, but it also correlates quite strongly with exercise performance (6-minute walking test), breathlessness in daily life (MRC breathlessness score) and disturbances of mood (anxiety and depression). The Impacts score is, therefore, the broadest component of the questionnaires, covering the whole range of disturbances that respiratory patients experience in their lives.

Three component scores are calculated: Symptoms; Activity; Impacts
One Total score is also calculated.

PRINCIPLE OF CALCULATION
Each questionnaire response has a unique empirically derived 'weight'. The lowest possible weight is zero and the highest is 100.
Each component of the questionnaire is scored separately in three steps:
i. The weights for all items with a positive responses are summed.
ii The weights for missed items are deducted from the maximum possible weight for each component. The weights for all missed items are deducted from the maximum possible weight for the Total score.
iii. The score is calculated by dividing the summed weights by the adjusted maximum possible weight for that component and expressing the result as a percentage:
Score = 100 x Summed weights from positive items in that component /Sum of weights for all items in that component

The Total score is calculated in similar way:
Score = 100 x Summed weights from positive items in the questionnaire/Sum of weights for all items in the questionnaire

Sum of maximum possible weights for each component and Total:

Symptoms	662.5
Activity	1209.1
Impacts	2117.8
Total	3989.4

(Note: these are the maximum possible weights that could be obtained for the worst possible state of the patient). For more details see: http://www.healthstatus.sgul.ac.uk/SGRQ_download/SGRQ%20Manual%20June%202009.pdf

IPF pharmacological treatments ongoing at enrollment
IPF pharmacological treatments from diagnosis and ogoing at enrollment will be defined as follows.
All IPF pharmacological treatments having (Start date of therapy (dd/mmm/yyyy) **[F23_IPF_PHARMACOLOGICAL_THERAPY.START_DATE_THER]** >= date of first IPF diagnosis (mm/yyyy) **[F05_DIAGNOSIS_IPF.DIA_Date_IPF_diagnosis]** AND Start date of therapy (dd/mmm/yyyy) < Date of enrollment visit) AND (end date (dd/mmm/yyyy) **[F23_IPF_PHARMACOLOGICAL_THERAPY.END_DATE_THER]** > Date of enrollment visit (dd/mmm/yyyy) **[_PatientInfo.Date_enrollment]** OR (end date missing AND "Ongoing at the end of observation?" = "Yes")) will be considered.
Drug names will be coded by CDM in actives.

IPF pharmacological treatments ongoing at 3, 6 and 12-month follow-up visit
IPF pharmacological treatments from diagnosis and ogoing at 3-, 6- or 12-month follow up will be defined as follows.
At each follow-up visit all treatments having (start date **[F23_IPF_PHARMACOLOGICAL_THERAPY.START_DATE_THER]** >= date of first IPF diagnosis (mm/yyyy) **[F05_DIAGNOSIS_IPF.DIA_Date_IPF_diagnosis]** AND < date of follow-up visit) AND ((end date **[F23_IPF_PHARMACOLOGICAL_THERAPY.END_DATE_THER]** >= date of first IPF diagnosis (mm/yyyy) **[F05_DIAGNOSIS_IPF.DIA_Date_IPF_diagnosis]** AND end date > date of follow-up visit **[F16_PATIENT_DISPOSITION.PD_2]**) OR (end date = missing and "Ongoing at the end of observation?" = "Yes" **[F23_IPF_PHARMACOLOGICAL_THERAPY.ONGOING_THER]**) will be selected.

IPF non-pharmacological therapy ongoing at enrollment

IPF non pharmacological treatments from diagnosis and ogoing at enrollment will be defined as follows.

All IPF non-pharmacological therapy having (Start date of therapy (dd/mmm/yyyy) **[F24_NON_PHARMACOLOGICAL_THERAPY. START_DATE_NF]** >= date of first IPF diagnosis (mm/yyyy) **[F05_DIAGNOSIS_IPF.DIA_Date_IPF_diagnosis]** AND Start date of therapy (dd/mmm/yyyy) < Date of enrollment visit) AND (end date (dd/mmm/yyyy) **[F24_NON_PHARMACOLOGICAL_THERAPY.END_DATE_NF]** > Date of enrollment visit (dd/mmm/yyyy) **[_PatientInfo.Date_enrollment]**) OR (missing and "Ongoing at the end of observation?" **[F24_NON_PHARMACOLOGICAL_THERAPY.ONGOING_NF_THER]** = "Yes")) will be considered.

For patients receiving more than one therapy, combination of therapies will be reported (e.g. Long-term oxygen therapy + Cardiopulmonary exercise training).

IPF non pharmacological treatments ongoing at 3-, 6- and 12-month follow-up visit

IPF non pharmacological treatments from diagnosis and ogoing at 3-, 6- or 12-month follow up will be defined as follows.

At each follow-up visit all treatments having (start date **[F24_NON_PHARMACOLOGICAL_THERAPY.START_DATE_NF]** >= date of first IPF diagnosis (mm/yyyy) **[F05_DIAGNOSIS_IPF.DIA_Date_IPF_diagnosis]** AND < date of follow-up visit) AND

((end date **[F24_NON_PHARMACOLOGICAL_THERAPY.END_DATE_NF]** >= date of first IPF diagnosis (mm/yyyy) **[F05_DIAGNOSIS_IPF.DIA_Date_IPF_diagnosis]** AND end date > date of follow-up visit **[F16_PATIENT_DISPOSITION.PD_2]** OR (end date = missing and "Ongoing at the end of observation?" = "Yes") **[F24_NON_PHARMACOLOGICAL_THERAPY.ONGOING_NF_THER])** will be selected.

Patients with AEs or ADRs during observation period

Are defined as patients with at least one AEs or ADRs between diagnosis and end of observation defined as events with date of diagnosis <= start date AE <= date of last available follow up.

4 CONTENTS

The tables to be produced for interim report are in green (if analysis of follow up data is planned, data collected up to 3-month follow up will be considered).
Missing data will not be imputed and so patients with missing data will be excluded from the analyses of that variable(s).
If the investigator is unable to collect the requested information the data will be "NK" (Not Known) or "NA" (Not Available), if the investigator did not record the information the data will be "Not Recorded".

4.1 Patient disposition

Table 1. Enrolled and evaluable patients
The table will provide absolute and relative frequencies of:

- patients enrolled in the FIBRONET study
- patients evaluable at enrollment (as described in par. 2.1)
- patients who performed V2 (3 ± 1.5 months)
- patients who performed V3 (6 ± 1.5 months)
- patients who performed V4 (9 ± 1.5 months)
- patients who performed V5 (12 ± 1.5 months)

The percentages will be computed over the total number of enrolled patients.

Table 2. Reasons for non-eligibility to analyses
The table will describe the reasons for patient non-eligibility at enrollment.
Absolute and relative frequency distribution will be performed; the percentages will be computed out of the total number of enrolled patients.

Table 3. Premature study termination

The table will describe the distribution of patients withdrawn from the study ("Did the patient complete the study?" **[F19_STUDY_COMPLETION.SC_1]** = "No") and the reasons for premature study termination ("Cause of drop out" **[F19_STUDY_COMPLETION.SC_2]**).

Absolute and relative frequency distribution will be performed; as for withdrawal, percentages will be computed out of the total number of patients evaluable at enrollment.

As regards reasons of withdrawal, the percentages will be computed out of the total number of patients withdrawn from the study. A patient could withdraw from the study for more than one reason.
The distribution of patients withdrawn for other reasons will be also reported in a separate table ("If other cause, specify:" ≠ missing **[F19_STUDY_COMPLETION.SC_3]**), if other reason frequency will be >20%.

Table 4. Months between baseline and follow up visits
The table will provide main descriptive statistics (mean, median, standard deviation, quartiles, min, max) of time (months) between baseline and each follow up visit.
Patients who performed each follow up visit will be considered.

4.2 Socio-demographics and clinical characteristics at enrollment

Table 5. Socio-demographic characteristics at enrollment
The table will provide:

- Main descriptive statistics (mean, median, standard deviation, quartiles, min, max) of patients' Age at enrollment (**[_PatientInfo.Age]**)
- Patient distribution by Gender (**[_PatientInfo.Gender]**)
- Patient distribution by Race (**[F02_SOCIO_DEMOGRAPHICS.SD_Race]**)
- Patient distribution by Highest education level at baseline (**[F02_SOCIO_DEMOGRAPHICS. SD_Education]**)
- Patient distribution by Employment status at baseline (**[F02_SOCIO_DEMOGRAPHICS. SD_Employment]**)
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Statistics will be computed out of the total number of patients evaluable at enrollment.

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4.4 Primary objective: Clinical course of IPF during observation

Table 13. IPF symptoms

The table will provide at enrollment and at V2, V3, V4, V5:

- Frequency distribution of patients with at least one IPF symptom **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms_YN]**
- Frequency distribution of IPF symptoms **[F06_IPF_SYMPTOMS.SYM_IPF_symptoms]**

Descriptives will be computed out of the total number of patients who performed the specific visit.

Table 20. Lung Function Assessments – Spirometry at each study visit and variation during observation period
The table will provide at enrollment, V2, V3, V4, V5 main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of:

- FEV1 (L) **[F07_LUNG_FUNCTION_ASS.LU_FEV1]**
- FEV1 of the predicted (%) **[F07_LUNG_FUNCTION_ASS.LU_FEV1_predicted]**
- FVC (L) **[F07_LUNG_FUNCTION_ASS. LU_FVC]**
- FVC of the predicted (%)
- FEV1/FVC (%) **[F07_LUNG_FUNCTION_ASS.LU_FEV1_FVC]**

- Total lung capacity (L) **[F07_LUNG_FUNCTION_ASS.LU_TLC_Num]**
- DLCO **[F07_LUNG_FUNCTION_ASS.LU_DLCO_Num]**, along with the respective DLCO unit **[F07_LUNG_FUNCTION_ASS.LU_DLCO_unit]**.
- DLCO of the predicted (%) **[F07_LUNG_FUNCTION_ASS.LU_DLCO_Predicted_Num]**
- SaO2 (%) **[F07_LUNG_FUNCTION_ASS.LU_SAO2 _Num]**
- change at each follow-up visit vs baseline of FEV1 (L)
- change at each follow-up visit vs baseline of FEV1 of the predicted (%)
- change at each follow-up visit vs baseline of FVC (L)
- (absolute and relative) change at each follow-up visit vs baseline of FVC of the predicted (%)
- change at each follow-up visit vs baseline of FEV1/FVC (%)

- change at each follow-up visit vs baseline of Total lung capacity (L)
- change at each follow-up visit vs baseline of DLCO, along with the respective DLCO unit
- change at each follow-up visit vs baseline of DLCO of the predicted (%)
- change at each follow-up visit vs baseline of SaO2 (%)

Evaluable patients at the specific visit with spirometry performed **[F07_LUNG_FUNCTION_ASS.LU_spirometry_YN]** at study visit or in the previous 3 months will be considered.

Table 21. Lung Function Assessments – Emogas analysis at each study visit and variation during observation period
The table will provide at enrollment, V2, V3, V4, V5 the main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of:

- PO2 (mmHg) **[F07_LUNG_FUNCTION_ASS.LU_PO2 _Num]**
- PaO2 (mmHg) **[F07_LUNG_FUNCTION_ASS.LU_PaO2 _Num]**
- PCO2 (mmHg) **[F07_LUNG_FUNCTION_ASS.LU_PCO2 _Num]**
- PaCO2 (mmHg) **[F07_LUNG_FUNCTION_ASS.LU_PaCO2 _Num]**
- change at each follow-up visit vs baseline vs PO2 (mmHg)
- change at each follow-up visit vs baseline vs PaO2 (mmHg)
- change at each follow-up visit vs baseline vs PCO2 (mmHg)
- change at each follow-up visit vs baseline vs PaCO2 (mmHg)

Evaluable patients at the specific visit with emogas analysis performed **[F07_LUNG_FUNCTION_ASS.LU_emogas_YN]** at study visit or in the previous 3 months will be considered.

Table 22. Lung Function Assessments – 6-minute walked distance test at each study visit and variation during observation period
The table will provide at enrollment, V2, V3, V4, V5 the main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of:

- Start SpO2 (%) **[F07_LUNG_FUNCTION_ASS.START_SPO2_Num]**
- 6-minute walked distance (m) **[F07_LUNG_FUNCTION_ASS.LU_6_minute_distance_Num]**
- SpO2 at the end of the test (%)**[F07_LUNG_FUNCTION_ASS.END_SpO2_Num]**
- test duration **[F07_LUNG_FUNCTION_ASS.LU_Time_stopped_Min, LU_Time_stopped_Sec]**. Minutest and seconds fields will be merged, and test duration will be expressed in minutes (seconds will be divided by 60).
- change in 6 minute walked distance test duration at each follow-up visit vs baseline. Minutes and seconds fields will be merged, and test duration will be expressed in minutes (seconds will be divided by 60).

The table will be provided overall and stratified by patients with test performed with O2 and without O2 **[F07_LUNG_FUNCTION_ASS.LU_6_minute_test].**

Evaluable patients at the specific visit with test performed **[F07_LUNG_FUNCTION_ASS.LU_6_minute_YN]** at study visit or in the previous 3 months will be considered.

4.6 Secondary objective #2: Frequency of exacerbations during observation

Table 24. Exacerbations since IPF diagnosis
This table will describe the absolute and relative frequency distribution of patients with:

- at least one exacerbation during observation period since IPF diagnosis **[F08_EXACERBATIONS.EX_Exacerbation_YN]**
- at least one mild, moderate, severe exacerbation during observation period since IPF diagnosis **[F08_EXACERBATIONS.Ex_exacer_1-10_Severity]**

Percentages will be computed out of the total number of patients evaluable at enrollment.

The table will provide the descriptive statistics (mean, median, standard deviation, quartiles, min, max) of

- number of exacerbations per patient since IPF diagnosis during observation period *(as defined in "Computed variables" chapter)*
- number of exacerbations per patient since IPF diagnosis during observation period stratified by exacerbation severity **[F08_EXACERBATIONS.Ex_exacer_1-10_Severity]**

Descriptives will be calculated out of the number of patients evaluable at enrollment.

4.7 Secondary objective #3: Health related quality of life (HRQoL) variation during 12 months of observation

Table 26. EQ-5D-5L distribution of items of descriptive system and VAS during observation
The table will provide at enrollment, V3, V5:

- Frequency or the proportion of reported problems for each level for each dimension: mobility, self-care, usual activity, pain/discomfort, anxiety/depression **[F11_EQ_5D_5L.EQ_5d_1-EQ_5D_5]**
- main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of EQ VAS **[F11_EQ_5D_5L.EQ_5d_6_NUM]**

Descriptives will be calculated over the number of patients who performed each visit with EQ-5D-5L filled in.
Higher index and VAS scores mean better QoI.

Table 27. St.Georges Respiratory Questionnaire (SGRQ)
The table will provide at enrollment, V3, V5 the descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the:

- 3 components scores of SGRQ: symptoms, activities and impacts on daily life;
- total score (as defined in "Computed variables" chapter).
- change at each follow-up visit vs baseline of symptoms, activities and impacts on daily life scores;
- change at each follow-up visit vs baseline of total score.

Descriptives will be calculated over the number of patients who performed each visit with SGRQ filled in.

4.8 Secondary objective #4: Healthcare resource utilization from diagnosis up to the end of 12-month follow-up

Table 28. Hospitalizations (inward/day hospital) and ICU admissions for IPF, IPF EXACERBATIONS OR IPF-RELATED ADVERSE EVENTS
The table will provide the distribution of patients with at least

- one hospitalization (inward/day hospital) ***[F20_RESOURCE_CONS.RES_Hosp_matrix_1__Inw- RES_Hosp_matrix_12__Inw]***
- one ICU admission ***[F20_RESOURCE_CONS. RES_Hosp_matrix_1__ICU_YN- RES_Hosp_matrix_12__ICU_YN]***

for IPF, IPF exacerbations or IPF related adverse events from diagnosis to the end of observation period.
Analyses will be computed out of the total number of patients evaluable at enrollment.

Table 29. Number of hospitalizations (inward/day hospital) and admissions to ICU and Overall duration of admission
The table will provide the distribution of patients by number of hospitalizations received from diagnosis to the end of observation period by type of admission (inward/day hospital) and number of admissions to ICU.
Analyses will be computed out of the total number of patients evaluable at enrollment.

The table will provide the descriptive statistics (mean, median, standard deviation, quartiles, min, max) of overall duration of admissions ***[F20_RESOURCE_CONS.RES_Hosp_matrix_1__Adm,RES_Hosp_matrix_12__Adm;F20_RESOURCE_CONS.RES_Hosp_matrix_1__adm_icu- RES_Hosp_matrix_12__adm_icu].***
Statistics computed over the total number of admissions received since IPF diagnosis till end of observation period, overall and stratified by type of admission (inward/day hospital, ICU).
Analyses will be computed out of the total number of patients evaluable at enrollment.

Table 30. Emergency room accesses
The table will provide

- Distribution of patients with at least one emergency room access for IPF, IPF exacerbations or IPF related adverse events from diagnosis to the end of observation period ***[F20_RESOURCE_CONS.RES_ER_YN];***
- Distribution of patients by number of ER accesses per patient ***[F20_RESOURCE_CONS.RES_ER_Matrix_1__n_acc-RES_ER_Matrix_8__n_acc]*** from diagnosis to the end of observation period.

Statistics computed over the total number of ER admissions received from diagnosis to the end of observation period.
Analyses will be computed out of the total number of patients evaluable at enrollment.

Table 31. Specialist and general practitioner outpatient visits
The table will provide

- Distribution of patients with at least one specialist or general practitioner outpatient visit for IPF, IPF exacerbations or IPF related adverse events ***[F20_RESOURCE_CONS.RES_OUTP_YN]*** from diagnosis to the end of observation period;
- Distribution of patients by type of specialist outpatient visits ***[F20_RESOURCE_CONS.Specialist, RES_other_Specialist]*** performed from diagnosis to the end of observation period. One patient could perform more than one type of specialist outpatient visit. A patient who performed the same type of visit more than once will count one.
- Descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the number of specialist outpatient visits per patient (overall and by visit type) ***[F20_RESOURCE_CONS.RES_Nr_Visits]*** from diagnosis to the end of observation period.

- Descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the number of GP visits for IPF, IPF exacerbations or IPF related adverse events per patient ***[F20_RESOURCE_CONS.RES_GP_Visit_YN_Num]*** from diagnosis to the end of observation period.

Analyses will be computed out of the total number of patients evaluable at enrollment.

Table 32. Patients who performed laboratory tests

The table will provide

- Distribution of patients with at least one laboratory test for IPF, IPF exacerbations or IPF related adverse events from diagnosis to the end of observation period ***[F20_RESOURCE_CONS.RES_LAB_TEST_YN]***

Analyses will be computed out of the total number of patients evaluable at enrollment.

Table 33. Laboratory tests: number and type

The table will provide

- Descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the number of laboratory tests per patient ***[F20_RESOURCE_CONS.RES_LAB_matrix_1_ex- RES_LAB_matrix_10_ex; F20_RESOURCE_CONS.RES_LAB_matrix_1_num- RES_LAB_matrix_10_num]*** from diagnosis to the end of observation period, overall and stratified by type of test/examination.

Analyses will be computed out of the total number of patients evaluable at enrollment.

4.9 Ongoing therapies for IPF

Table 34. IPF treatments ongoing at enrollment

The table will provide:

- Frequency distribution of patients with at least one IPF pharmacological treatment ongoing at baseline **[F09_THERAPY_IPF. THER_Pharma_YN].**
- Frequency distribution of patients with at least one IPF non pharmacological treatment ongoing at baseline **[F09_THERAPY_IPF. THER_non_pharma_YN].**
- Frequency distribution of patients listed for lung transplantation at enrollment **[F09_THERAPY_IPF. THER_transplant_YN]**.

stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).

Percentages will be computed out of the total number of patients evaluable at enrollment.

Table 35. IPF treatments ongoing at 3-month follow up

The table will provide:

- Frequency distribution of patients with at least one IPF pharmacological treatment ongoing at 3-month follow up.
- Frequency distribution of patients with at least one IPF non pharmacological treatment ongoing at 3-month follow up.
- Frequency distribution of patients listed for lung transplantation at 3-month follow up **[F09_THERAPY_IPF. THER_transplant_fup_YN]**.

stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).

Percentages will be computed out of the total number of patients who performed the 3-month follow up.

Table 36. IPF treatments ongoing at 6-month follow up

The table will provide:

- Frequency distribution of patients with at least one IPF pharmacological treatment ongoing at 6-month follow up.
- Frequency distribution of patients with at least one IPF non pharmacological treatment ongoing at 6-month follow up.
- Frequency distribution of patients listed for lung transplantation at 6-month follow up **[F09_THERAPY_IPF. THER_transplant_fup_YN]**.

stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).

Percentages will be computed out of the total number of patients who performed the 6-month follow up.

Table 37. IPF treatments ongoing at 12-month follow up

The table will provide:

- Frequency distribution of patients with at least one IPF pharmacological treatment ongoing at 12-month follow up.
- Frequency distribution of patients with at least one IPF non pharmacological treatment ongoing at 12-month follow up.
- Frequency distribution of patients listed for lung transplantation at 12-month follow up **[F09_THERAPY_IPF. THER_transplant_fup_YN]**.

stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).

Percentages will be computed out of the total number of patients who performed the 12-month follow up.

4.10 Ongoing pharmacological therapies for IPF

Table 38. Distribution of patients according to IPF pharmacological treatments ongoing at enrollment
The table will provide the frequency distribution of IPF pharmacological treatments (actives) ongoing at enrollment (see 'Computed variables' chapter) stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).
A patient could receive more than one active.
Percentages will be computed out of the total number of patients evaluable at enrollment.

Table 39. Distribution of patients according to IPF pharmacological treatments ongoing at 3-month follow up
The table will provide the frequency distribution of IPF pharmacological treatments (actives) ongoing at 3-month follow up (see 'Computed variables' chapter) stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).
A patient could receive more than one active.
Percentages will be computed out of the total number of patients who performed the 3-month follow up.

Table 40. Distribution of patients according to IPF pharmacological treatments ongoing at 6-month follow-up visit
The table will provide the frequency distribution of IPF pharmacological treatments (actives) ongoing at 6-month follow up (see 'Computed variables' chapter) stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).
A patient could receive more than one active.
Percentages will be computed out of the total number of patients who performed the 6-month follow up.

Table 41. Distribution of patients according to IPF pharmacological treatments ongoing at 12-month follow-up visit
The table will provide the frequency distribution of IPF pharmacological treatments (actives) ongoing at 12-month follow up (see 'Computed variables' chapter) stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).
A patient could receive more than one active.
Percentages will be computed out of the total number of patients who performed the 12-month follow up.

Table 42. IPF pharmacological treatments from diagnosis to the end of observation period – Dosage regimen
The table will consider all the pharmacological treatments assumed by the patients for IPF, IPF-exacerbations or IPF-related AEs from diagnosis to the end of observation period. It will provide:
Descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the IPF pharmacological treatment dosage per administration by Drug, Unit of administration, frequency of administration [**F23_IPF_PHARMACOLOGICAL_THERAPY.DRUG, UNIT_3,FREQ_ADMN**] and duration of therapy (number of days).
Two separate tables wil be provided: one for IPF pharmacological treatments ongoing at enrollment having/not having fixed-dose formulation [**F23_IPF_PHARMACOLOGICAL_THERAPY.DOSE_2**].
The patients evaluable at enrollment will be considered.

Table 43. Time between diagnosis and start of therapy for IPF
The table will provide the main descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the time between diagnosis and start of therapy for IPF (weeks).
First therapy for IPF assumed by evaluable patients will be considered.
Only therapies for IPF will be considered.

4.11 Pharmacological therapies for IPF and exacerbations

Listing 44. Patients with exacerbations during observational period and therapy for IPF
A listing of patients with at least one exacerbation during observational period will be shown. The therapy ongoing before the exacerbation and the therapy ongoing after the exacerbation will be shown; in case of no therapy, this will be indicated in the listing.
In case of more than one exacerbation all the above information (about therapy before and after the exacerbation) will be shown referring to each exacerbations.

4.12 Ongoing non pharmacological therapies for IPF

Table 45. IPF non pharmacological therapy ongoing at enrollment
The table will provide the frequency distribution of IPF non pharmacological therapies (long-term oxygen therapy, cardiopulmonary exercise training or psychological support) ongoing at enrollment (see 'Computed variables' chapter) stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).
Percentages will be computed out of the total number of patients evaluable at enrollment.

Table 46. Distribution of patients according to IPF non pharmacological therapy ongoing at 3-month follow up
The table will provide the frequency distribution of IPF non pharmacological therapies (long-term oxygen therapy, cardiopulmonary exercise training or psychological support) ongoing at 3-month follow-up visit (see 'Computed variables' chapter) stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).
Percentages will be computed out of the total number of patients who performed the 3-month follow up.

Table 47. Distribution of patients according to IPF non pharmacological therapy ongoing at 6-month follow-up visit
The table will provide the frequency distribution of IPF non pharmacological therapies (long-term oxygen therapy, cardiopulmonary exercise training or psychological support) ongoing at 6-month follow-up visit (see 'Computed variables' chapter) stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).
Percentages will be computed out of the total number of patients who performed the 6-month follow up.

Table 48. Distribution of patients according to IPF non pharmacological therapy ongoing at 12-month follow-up visit
The table will provide the frequency distribution of IPF non pharmacological therapies (long-term oxygen therapy, cardiopulmonary exercise training or psychological support) ongoing at 12-month follow-up visit (see 'Computed variables' chapter) stratified by type of therapy (therapy for IPF, IPF-exacerbations or IPF-related AEs).
Percentages will be computed out of the total number of patients who performed the 12-month follow up.

Table 49. IPF non pharmacological therapy from diagnosis to the end of observation period – Number of sessions of cardiopulmonary exercise training or psychological support
It will provide the descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the total number of sessions of cardiopulmonary exercise training or psychological support performed from diagnosis to the end of observation period [**F24_NON_PHARMACOLOGICAL_THERAPY.N_SESSIONS**] by therapy [**F24_NON_PHARMACOLOGICAL_THERAPY.THERAPY**].
The patients evaluable at enrollment will be considered.

Table 50. Long term Oxygen therapy from diagnosis to the end of observation period – Dosage regimen
The table will consider all the long-term oxygen therapies assumed by the patients for IPF, IPF-exacerbations or IPF_related AES from diagnosis to the end of observation period.
It will provide the descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the flow (L/min) [**F24_NON_PHARMACOLOGICAL_THERAPY.FLOW]** by Drug **[F24_NON_PHARMACOLOGICAL_THERAPY.DRUG],** Hours per day **[F24_NON_PHARMACOLOGICAL_THERAPY.HOURS**] and duration of therapy (number of days).
The patients evaluable at enrollment will be considered.

4.14 AEs and ADRs between diagnosis and end of observation

Table 52. Patients with AEs and ADRs between diagnosis and end of observation
The table will provide the absolute and relative frequency of the patients with at least one adverse events between diagnosis and end of observation.
The total number of evaluable patients at enrollment will be considered.

Listing 53. AEs and ADRs between diagnosis and end of observation
The table will provide the distribution of every AE or ADR, occurred between diagnosis and end of observation by serious AE, seriousness category and causal relationship with Nintedanib.
The total number of evaluable patients at enrollment will be considered.

4.15 Appendix

Table A3. Methods of diagnosis (by HRCT findings)
The table will provide the distribution of methods of evaluable patients according to methods of diagnosis crosstabulated by HRCT finding compatible with current ATS/ERS criteria.
The table will be provided considering patients evaluable at enrollment.

Table A4. IPF treatments ongoing at enrollment (Patients with IPF symptoms at baseline and no symptoms at 3-month follow up)
The table will provide the frequency distribution of patients with at least one pharmacological therapy for IPFongoing at enrollment.
The patients with IPF symptoms at baseline and no symptoms at 3-month follow up will be considered.
The table will be provided at V3 and V5.

Table A5. Distribution of patients according to IPF pharmacological treatments ongoing at enrollment (Patients with IPF symptoms at baseline and no symptoms at 3-month follow up)
The table will provide the frequency distribution of patients according to IPF pharmacological treatments ongoing at enrollment.
The patients with IPF symptoms at baseline and no symptoms at 3-month follow up will be considered.
The table will be provided at V3 and V5.

Table A6. IPF treatments ongoing at 3-month follow up (Patients with IPF symptoms at baseline and no symptoms at 3-month follow up)
The table will provide the frequency distribution of patients with at least one pharmacological therapy for IPF ongoing at 3-month follow up.
The patients with IPF symptoms at baseline and no symptoms at 3-month follow up.
The table will be provided at V3 and V5.

Table A7. Distribution of patients according to IPF pharmacological treatments ongoing at 3-month follow up (Patients with IPF symptoms at baseline and no symptoms at 3-month follow up)
The table will provide the frequency distribution of patients according to IPF pharmacological treatments ongoing at 3-month follow up.
The patients with IPF symptoms at baseline and no symptoms at 3-month follow up will be considered.
The table will be provided at V3 and V5.