Zephyrus II: Efficacy and Safety Study of Pamrevlumab in Subjects With Idiopathic Pulmonary Fibrosis (IPF)

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Main Information

Primary registry identifying number
LBCTR2020094566

Protocol number
FGCL-3019-095

MOH registration number
30220/2020

Study registered at the country of origin
No

Study registered at the country of origin: Specify
No

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency
08/09/2020

Primary sponsor
FibroGen Inc.

Primary sponsor: Country of origin
United States of America

Date of registration in primary registry
11/10/2021

Date of registration in national regulatory agency
08/09/2020

Public title
Zephyrus II: Efficacy and Safety Study of Pamrevlumab in Subjects With Idiopathic Pulmonary Fibrosis (IPF)

Acronym

Scientific title
Zephyrus II: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Efficacy and Safety Study of Pamrevlumab in Subjects with Idiopathic Pulmonary Fibrosis (IPF)

Acronym

Brief summary of the study: English
This is a Phase 3 trial to evaluate the efficacy and safety of 30 mg/kg intravenous (IV) infusions of pamrevlumab administered every 3 weeks as compared to placebo in subjects with Idiopathic Pulmonary Fibrosis

Brief summary of the study: Arabic
هذه تجربة Phase 3 -ل لتقييم فعالية وسلامة الحقن الوريدي 30من كجم / مجم Pamrevlumab كل3 عند أسابيع مقارنة بالدواء الوهمي
الأشخاص المصابين بالتليف الرئوي مجهول السبب

Health conditions/problem studied: Specify
Idiopathic Pulmonary Fibrosis

Interventions: Specify
*Drug: Pamrevlumab (FG-3019)
Pamrevlumab: 30 mg/kg by intravenous infusion every 3 weeks for a total of 17 infusions over 48 weeks

*Drug: Placebo
Placebo: 30 mg/kg by intravenous infusion every 3 weeks for a total of 17 infusions over 48 weeks

Key inclusion and exclusion criteria: Inclusion criteria
1. Age 40 to 85 years, inclusive, at screening initiation.
2. Diagnosis of IPF as defined by ATS/ERS/JRS/ALAT guidelines (Raghu 2018).

3. IPF diagnosis within the past 7 years, with onset defined as the date of the first recorded diagnosis of IPF by HRCT and/or surgical biopsy (SLB) or other appropriate tissue samples (e.g., cryobiopsy) in the medical history.
4. Interstitial pulmonary fibrosis defined by HRCT scan at Screening, with evidence of ≥10% to <50% parenchymal fibrosis (reticulation) and <25% honeycombing, within the whole lung. NOTE: this requires confirmation by an Independent Radiology Imaging Review Group, prior to randomization. If a recent HRCT scan (within 3 months prior to screening) is available, it can be utilized for screening purposes, provided it is submitted and evaluated by the Independent Radiology Imaging Review Group, is adhering to the imaging parameters detailed in the Imaging Core Manual (ICM), and is using the same accredited scanner as the on-study HRCT scans.
5. FVCpp value ≥50% and ≤80% at Screening and Day 1.
6. Diffusing capacity of the lungs for carbon monoxide (DLCO) percent predicted and corrected by Hb value ≥30% and ≤90% at Screening (determined locally).
7. Both FVC and DLCO testing must be representative of the IPF underlying disease (i.e. have been obtained in absence of an acute respiratory event [e.g. lung infection, cold] or other events that are known to affect PFT testing results [e.g., broken rib, chest pain, other]).
8. Previously treated with an approved IPF therapy (i.e., pirfenidone or nintedanib) but discontinued at least 1 week prior to screening, unless neither treatment is available in the host country. NOTE: no subject should discontinue approved therapy for the purpose of enrolling in this study.
9. Male subjects with partners of childbearing potential and female subjects of childbearing potential (including those <1 year postmenopausal) must use double barrier contraception methods during the conduct of the study, and for 3 months after the last dose of study drug. Women not of childbearing potential are defined as:
a. Post-menopausal women (defined as at least 12 months with no menses without an alternative medical cause); in women < 45 years of age, a high follicle-stimulating hormone (FSH) level in the post-menopausal range may be used to confirm a post-menopausal state in women not using hormonal contraception or hormonal replacement therapy; OR
b. Have had a hysterectomy and/or bilateral oophorectomy, bilateral salpingectomy, or bilateral tubal ligation/occlusion, at least 6 weeks prior to screening; OR
c. Have a congenital or acquired condition that prevents childbearing.
10. Able to understand and sign a written informed consent form.

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

40

Key inclusion and exclusion criteria: Age maximum

85

Key inclusion and exclusion criteria: Exclusion criteria

1. Previous exposure to pamrevlumab.
2. Evidence of significant obstructive lung disease by any of the following criteria: (1) forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) ratio <0.70, or (2) extent of emphysema greater than the extent of fibrosis on HRCT. NOTE: this requires confirmation by an Independent Radiology Imaging Review Group, prior to randomization.
3. Female subjects who are pregnant or nursing.
4. Smoking within 3 months of Screening and/or unwilling to avoid smoking throughout the study.
5. Interstitial lung disease (ILD) other than IPF, including but not limited to any of the other types of idiopathic interstitial pneumonia; lung diseases related to exposure to fibrogenic agents or other environmental toxins or drugs; other types of occupational lung diseases; granulomatous lung diseases; pulmonary vascular diseases; systemic diseases, including vasculitis, infectious diseases (i.e. TB) and connective tissue diseases. In cases of uncertain diagnosis, serological testing and/or review by the multi-disciplinary team should be performed to confirm the diagnosis of IPF vs. other types of ILD.
6. Sustained improvement in the severity of IPF during the 12 months prior to Screening, based on changes in FVC, DLCO, and/or HRCT scans of the chest.
7. History of other types of respiratory diseases, including diseases or disorders of the airways, lung parenchyma, pleural space, mediastinum, diaphragm, or chest wall that, in the opinion of the Investigator, would impact the primary protocol endpoint or otherwise preclude the subject's participation in the study.
8. Medical conditions (e.g. MI/stroke within the past 6 months), or logistical challenges that in the opinion of the Investigator preclude the subject's adequate participation in the study.
9. Poorly controlled chronic heart failure (NYHA Class 3 or above); clinical diagnosis of cor pulmonale requiring specific treatment; or severe pulmonary arterial hypertension requiring specific treatment that, in the opinion of the Investigator, would preclude the subject's participation in the study.
10. Clinically important abnormal laboratory tests (including serum creatinine ≥1.5 x upper limit of normal [ULN], hemoglobin (Hb) <10 g/dL, white blood cells <3,000/mm3, platelets less than 100,000/mm3, serum total bilirubin >1.5 x ULN, serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥2 x ULN, or serum alkaline phosphatase ≥2 x ULN.
11. Ongoing acute IPF exacerbation, or suspicion of such process by the Investigator, during Screening or Randomization.
12. High likelihood of lung transplantation (in the opinion of the Investigator) within 6 months after Day 1.
13. Use of any investigational drugs or unapproved therapies, or participation in any clinical trial with an investigational new drug within 30 days prior to screening.
14. Daily use of PDE-5 inhibitor drugs (e.g. sildenafil, tadalafil) except for treatment of severe pulmonary artery hypertension.
15. Any current malignancy (this does not include localized cancer such as basal or squamous cell carcinoma of the skin). Any history of malignancy likely to result in mortality, or requiring significant medical or surgical intervention within the next year.
16. History of allergic or anaphylactic reaction to human, humanized, chimeric or murine monoclonal antibodies.
17. Any condition (other than IPF) that is likely to result in the death of the patient within the next year.
18. The Investigator judges that the subject will be unable to fully participate in the study and complete it for any reason, including the inability to comply with study procedures and treatment, addiction, or any other relevant medical or psychiatric conditions.

Type of study

Interventional

Type of intervention
Pharmaceutical

Type of intervention: Specify type
N/A

Trial scope
Other

Trial scope: Specify scope

Study design: Allocation
Randomized controlled trial

Study design: Masking
Blinded (masking used)

Study design: Control
Placebo

Study phase
3

Study design: Purpose
Treatment

Study design: Specify purpose
N/A

Study design: Assignment
Parallel

Study design: Specify assignment
N/A

IMP has market authorization
No

IMP has market authorization: Specify

Name of IMP
Pamrevlumab (FG-3019)

Year of authorization

Month of authorization

Type of IMP
Others

Pharmaceutical class
Pamrevlumab is a recombinant fully human immunoglobulin G1 (IgG) kappa monoclonal antibody that binds to connective tissue growth factor (CTGF)

Therapeutic indication
Idiopathic Pulmonary Fibrosis

Therapeutic benefit
Pamrevlumab is a recombinant fully human immunoglobulin G1 (IgG1) kappa monoclonal antibody which inhibits the activity of connective tissue growth factor (CTGF).

Study model
N/A

Study model: Explain model
N/A

Study model: Specify model
N/A

Time perspective
N/A

Time perspective: Explain time perspective
N/A

Time perspective: Specify perspective
N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention
Samples without DNA

Biospecimen description
Samples with DNA is optional

Target sample size
7

Actual enrollment target size

Date of first enrollment: Type
Anticipated

Date of first enrollment: Date
15/10/2020

Date of study closure: Type
Anticipated

Date of study closure: Date
30/06/2023

Recruitment status
Pending

Recruitment status: Specify

Date of completion
31/03/2023

IPD sharing statement plan
No

IPD sharing statement description
Confidential Info

Additional data URL

Admin comments

Trial status
Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
ClinicalTrials.gov	NCT04419558
EU Clinical Trials Register	2020-000697-22

Sources of Monetary or Material Support

Name
FibroGen Inc.- USA

Secondary Sponsors

Name
N/A

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Dr. Samer Kabbani	Beirut	Lebanon	9611744772	kabbanisamer@hotmail.com	Rafik Hariri University Hospital
Scientific	Dr. Moussa Riachi	Beirut	Lebanon	96116150755	moussariachy@gmail.com	Hotel Dieu de France Hospital

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu de France Hospital	Dr. Moussa Riachy	Pulmonary Medicine	Approved
Rafic Hariri University Hospital	Dr. Samer Kabbani	Cardiology	Approved
American University of Beirut Medical Center	Dr. Pierre Bou Khalil	Internal Medicine	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hotel Dieu de France	05/05/2020	Pr. Sami Richa	cue@usj.edu.lb	+9611421229
Rafic Hariri University Hospital	03/06/2020	Dr. Iyad Issa	N/A	+9611830000
American University of Beirut Medical Center	30/12/2020	Dr. Fuad Ziyadeh	NA	+9611350000

Countries of Recruitment

Name
France
Lebanon
Italy
Hungary
Netherlands
Germany
United Kingdom
Spain
Denmark
Czech Republic
Georgia
Hungary

Health Conditions or Problems Studied

Condition	Code	Keyword
Idiopathic Pulmonary Fibrosis	Other diseases of pulmonary vessels (I28)	Idiopathic Pulmonary Fibrosis IPF Idiopathic Interstitial Pneumonia Interstitial Lung Disease Lung Fibrosis, Pulmonary Fibrosis Idiopathic Pulmonary Fibrosis Fibrosis Pathologic Processes, Lung Diseases Respiratory Tract Diseases Idiopathic Interstitial Pneumonias Lung Diseases, Interstitial

Interventions

Intervention	Description	Keyword
Drug	Pamrevlumab	FG-3019
Drug	Placebo	N/A

Primary Outcomes

Name	Time Points	Measure
Proportion of subjects with Disease Progression	Baseline to Week 52	absolute FVC percent predicted (FVCpp) decline of ≥10% or death

Key Secondary Outcomes

Name	Time Points	Measure
Change in FVC (L)	Baseline to Week 52	FVC (L)
Change in FVCpp	Baseline to Week 52	Change in FVCpp (absolute and relative)
Composite of clinical outcomes	Baseline to Week 52	Respiratory hospitalization or death or absolute FVCpp decline ≥10%, whichever occurs first
Respiratory hospitalizations	Baseline to Week 52	Respiratory hospitalizations
Change in Quantitative Lung Fibrosis (QLF) volume	Baseline to Week 52	Quantitative Lung Fibrosis (QLF) volume
Change in St. George's Respiratory Questionnaire (SGRQ) score	Baseline to Week 48	St. George's Respiratory Questionnaire (SGRQ) score
Change in University of California San Diego – Shortness of Breath Questionnaire (UCSD-SOBQ) score	Baseline to Week 48	University of California San Diego – Shortness of Breath Questionnaire (UCSD-SOBQ) score
Change in Leicester Cough Questionnaire (LCQ)	Baseline to Week 48	Leicester Cough Questionnaire (LCQ)
All-cause mortality	During whole study duration	Death
Acute IPF exacerbations	During whole study duration	N/A

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files