Phase 3 study to evaluate the efficacy and safety of human plasma-derived fibrinogen concentrate (FIB Grifols) in subjects with congenital afibrinogenaemia and severe hypofibrinogenemia

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Main Information

Primary registry identifying number
LBCTR2021024523

Protocol number
GC1801

MOH registration number

Study registered at the country of origin
No

Study registered at the country of origin: Specify
NA

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency
14/07/2020

Primary sponsor
Instituto Grifols, S.A.

Primary sponsor: Country of origin
Spain

Date of registration in primary registry
21/03/2021

Date of registration in national regulatory agency
14/07/2020

Public title
Phase 3 study to evaluate the efficacy and safety of human plasma-derived fibrinogen concentrate (FIB Grifols) in subjects with congenital afibrinogenaemia and severe hypofibrinogenemia

Acronym
NA

Scientific title
A prospective, multicenter, open-label, single-arm study to evaluate the efficacy and safety of human plasma-derived fibrinogen concentrate (FIB Grifols) in subjects with congenital afibrinogenaemia and severe hypofibrinogenemia requiring either ondemand treatment for acute bleeding or surgical prophylaxis

Acronym
NA

Brief summary of the study: English
This is a phase 3, multi-center, prospective, open-label, single-arm, clinical trial to be carried out in subjects with congenital fibrinogen deficiency manifested as afibrinogenemia or severe hypofibrinogenemia in order to evaluate the efficacy and safety of human plasma-derived fibrinogen concentrate (FIB Grifols)

Brief summary of the study: Arabic
هذه دراسة سريرية مستقبلية في المرحلة الثالثة، متعددة المراكز، مفتوحة التسمية, أحادية المجموعة يتم إجراؤها لدى الأشخاص الذين يعانون من نقص الفيبرينوجين الخلقي الذي يتجلى على أنه فبرينوجين الدم المنعدم أو نقص فيبرينوجين الدم الوخيم من أجل تقييم فعالية وسلامة مركز الفيبرينوجين المشتق من البلازما البشرية (FIB Grifols)

Health conditions/problem studied: Specify
Congenital fibrinogen deficiency (afibrinogenemia or severe hypofibrinogenemia)

Interventions: Specify

Experimental: FIB Grifols

FIB Grifols will be administered via slow intravenous (IV) infusion at a rate not to exceed 5 mL/minute.
Dosing will be individually calculated for each subject based on the target plasma fibrinogen level according to the type of bleeding, measured actual plasma fibrinogen level before infusion, and body weight. The IP will be administered according to the nominal potency of the product.

The duration of FIB Grifols treatment is 1 day with additional IV infusions administered according to daily assessments, clinical trial protocol guidance, and investigator's judgment.

Key inclusion and exclusion criteria: Inclusion criteria

A subject must meet all the following inclusion criteria to be eligible for participation in this study.
1. Male or female subject between 6 to 70 years of age.
2. Signed and dated written ICF, or the subject's parent or legal guardian signs and dates the ICF where applicable, and the Subject Authorization Form (SAF) where applicable. Pediatric subjects, as defined by local regulations, will be asked to sign an age appropriate assent form.
3. Diagnosed with congenital fibrinogen deficiency manifested as afibrinogenemia or severe hypofibrinogenemia (fibrinogen <50 mg/dL) and expected to require treatment for acute bleeding (either spontaneous or after trauma [defined as any accidental event leading to acute bleeding]), or prophylaxis of bleeding before a surgical intervention or invasive procedure.
4. Fibrinogen level < 50 mg/dL determined by Clauss method at baseline (sample drawn within 24 hours prior to infusion on Infusion 1 Day 1 Visit).
5. Female subjects of child-bearing potential must have a negative test for pregnancy blood or urine human chorionic gonadotropin (HCG)-based assay at baseline (sample drawn within 24 hours prior to infusion on Infusion 1 Day 1 Visit).
a. Female subjects/partners of child-bearing potential include any female who has experienced menarche and who has not undergone successful surgical sterilization (eg, hysterectomy, bilateral tubal ligation, or bilateral oophorectomy) or are not postmenopausal (post menopausal is defined as amenorrhea for >12 consecutive months or women on hormone replacement therapy with documented serum follicle stimulating hormone level <35 mIU/mL). Even women who are using oral, implanted or injectable contraceptive hormones, mechanical products such as an intrauterine device [IUD], or barrier methods (eg, diaphragm, condoms, spermicides) to prevent pregnancy, or are practicing abstinence or where their partner is sterile (eg, vasectomy), should be considered to be of child bearing potential.
6. Willing to comply with all aspects of the clinical trial protocol, including blood sampling, for the entire duration of the study.

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

6

Key inclusion and exclusion criteria: Age maximum

70

Key inclusion and exclusion criteria: Exclusion criteria

Exclusion Criteria
A subject meeting any of the following exclusion criteria is NOT eligible for participation in the study.
1. Has acquired (secondary) fibrinogen deficiency.
2. Diagnosed with dysfibrinogenemia.
3. Has known antibodies against fibrinogen.
4. Has history of anaphylaxis or severe systemic response to any drug or blood-derived product.
5. Has history of intolerance to any component of the IP.
6. Documented history of immunoglobulin A (IgA) deficiency and antibodies against IgA.
7. Is a female who is pregnant, breastfeeding or, if of child-bearing potential, unwilling to practice a highly effective method of contraception (eg, oral, injectable, or implantable hormonal methods of contraception, placement of an IUD or intrauterine system, condom or occlusive cap with spermicidal foam/gel/film/cream/suppository, male sterilization, or true abstinancea) throughout the study.
a. True abstinance: when this is in line with the preferred and usual lifestyle of the subject (Periodic abstinance [eg, calendar, ovulation, symptothermal, post-ovulation methods], declaration of abstinance for the duration of a trial, and withdrawal are not acceptable methods of contraception.
8. Has any medical condition which is likely to interfere with the evaluation of the IP and/or the satisfactory conduct of the clinical trial according to the investigator's judgment.
9. Has congenital or acquired bleeding disorders other than congenital fibrinogen deficiency.
10. Has life expectancy of less than 6 months.
11. Received FRT within 21 days prior to the Screening Visit.
12. Receiving, or having received within 3 months prior to the Screening Visit of this clinical trial, any investigational drug or device.
13. Is unlikely to adhere the protocol requirements, or is likely to be uncooperative, or unable to provide a storage sample prior to IP infusion.

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Trial scope: Specify scope

Therapy

N/A

Study design: Allocation

Single Arm Study

Study design: Masking

Open (masking not used)

Study design: Control

N/A

Study phase

3

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Single

Study design: Specify assignment

N/A

IMP has market authorization

No

IMP has market authorization: Specify

Name of IMP

FIB Grifols

Year of authorization

Month of authorization

Type of IMP

Plasma derived

Pharmaceutical class

Human plasma-derived fibrinogen concentrate

Therapeutic indication

Congenital fibrinogen deficiency (afibrinogenemia or severe hypofibrinogenemia)

Therapeutic benefit

The intended benefit of fibrinogen concentrates is to avoid hemorrhagic manifestations in subjects with congenital fibrinogen deficiency.

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

None retained

Biospecimen description

NA

Target sample size
32

Actual enrollment target size

Date of first enrollment: Type
Anticipated

Date of first enrollment: Date
12/10/2020

Date of study closure: Type
Anticipated

Date of study closure: Date
31/12/2023

Recruitment status
Pending

Recruitment status: Specify

Date of completion

IPD sharing statement plan
No

IPD sharing statement description
NA

Additional data URL

Admin comments

Trial status
Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Food and Drug Administration	IND number 15811

Sources of Monetary or Material Support

Name
Instituto Grifols, S.A.

Secondary Sponsors

Name
NA

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Aziz Zoghbi	MCT-CRO	Lebanon	+961 71 008 269	zog_az@mct-cro.com	Country Oversight and Management Africa, Levant and GCC
Scientific	Claudia Khayat	Hotel Dieu de France Hospital	Lebanon	+961 3 704 864	claudiakhayat@yahoo.fr	Principle Investigator

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu de France Hospital	Dr. Claudia Khayat	Pediatric Hematology/Oncology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hotel Dieu de France	30/06/2020	Nancy Alam	nancy.alam@usj.edu.lb	+961 1 421 000 ext 2335

Countries of Recruitment

Name
India
Bulgaria
Lebanon
Turkey
United States of America
United Kingdom

Health Conditions or Problems Studied

Condition	Code	Keyword
Congenital fibrinogen deficiency manifested as afibrinogenemia or severe hypofibrinogenemia	Fibrinolysis-affecting drugs (T45.6)	afibrinogenemia or severe hypofibrinogenemia

Interventions

Intervention	Description	Keyword
Experimental: FIB Grifols	FIB Grifols will be administered via slow intravenous (IV) infusion at a rate not to exceed 5 mL/minute. Dosing will be individually calculated for each subject based on the target plasma fibrinogen level according to the type of bleeding, measured actual plasma fibrinogen level before infusion, and body weight. The IP will be administered according to the nominal potency of the product. The duration of FIB Grifols treatment is 1 day with additional IV infusions administered according to daily assessments, clinical trial protocol guidance, and investigator's judgment.	FIB Grifols, IV

Primary Outcomes

Name	Time Points	Measure
overall clinical assessment of the hemostatic efficacy of FIB Grifols	In case of bleeding episode: At the end of treatment Observation period visit. In case of surgery: End of surgery and at the end of treatment observational period visit	The primary efficacy endpoint is the overall clinical assessment of the hemostatic efficacy of FIB Grifols in treating all documented acute bleeding episodes or in preventing excessive bleeding during and after all documented surgical procedures according to a 4-point scale. Hemostatic efficacy will be rated as excellent, good, moderate, or none. The primary efficacy endpoint will be assessed by the IEAC.

Key Secondary Outcomes

Name	Time Points	Measure
Overall clinical assessment of the hemostatic efficacy of FIB Grifols	In case of bleeding episode: At the end of treatment Observation period visit. In case of surgery: End of surgery and at the end of treatment observational period visit	Overall clinical assessment of the hemostatic efficacy of FIB Grifols in treating the first documented acute bleeding episode or in preventing excessive bleeding during and after the first documented surgical procedure according to a 4 point scale. This secondary efficacy endpoint will be assessed by the IEAC.
Overall clinical assessment of the hemostatic efficacy of FIB Grifols	In case of bleeding episode: At the end of treatment Observation period visit. In case of surgery: End of surgery and at the end of treatment observational period visit	Overall clinical assessment of the hemostatic efficacy of FIB Grifols in treating the first acute bleeding episode as assessed by the principal investigator at each trial site according to a 4-point scale
Overall clinical assessment of the hemostatic efficacy of FIB Grifols	In case of bleeding episode: At the end of treatment Observation period visit. In case of surgery: End of surgery and at the end of treatment observational period visit	Overall clinical assessment of the hemostatic efficacy of FIB Grifols in treating all acute bleeding episodes as assessed by the principal investigator at each trial site according to a 4-point scale
Overall clinical assessment of the hemostatic efficacy of FIB Grifols	In case of bleeding episode: At the end of treatment Observation period visit. In case of surgery: End of surgery and at the end of treatment observational period visit	Clinical assessment of the hemostatic efficacy of FIB Grifols in preventing excessive bleeding intra-operatively for all surgical procedures as assessed by the surgeon (defined as the licensed medical professional performing the invasive procedure [eg, dentist]) according to a 4-point scale
Overall clinical assessment of the hemostatic efficacy of FIB Grifols	In case of bleeding episode: At the end of treatment Observation period visit. In case of surgery: End of surgery and at the end of treatment observational period visit	Clinical assessment of the hemostatic efficacy of FIB Grifols in preventing excessive bleeding after all surgical procedures (ie, post-operative) as assessed by the principal investigator at each trial site according to a 4-point scale
Difference in MCF	From pre-infusion to 1 hour after the end of each infusion	Measured by ROTEM
Difference in MCF	From pre-infusion to 4 hours after the end of each infusion	Measured by ROTEM
Difference (improvement) in Thrombin Time	From pre-infusion to 1 hour after the end of each infusion	Difference (improvement) in Thrombin Time
Difference (improvement) in Prothrombin Time	From pre-infusion to 1 hour after the end of each infusion	Difference (improvement) in Prothrombin Time
Difference (improvement) in activated Partial Thromboplastin Time	From pre-infusion to 1 hour after the end of each infusion	Difference (improvement) in activated Partial Thromboplastin Time
Difference in plasma fibrinogen levels	From pre-infusion to 1 hour after the end of each infusion	By Clauss and ELISA
Difference in plasma fibrinogen levels	From pre-infusion to 4 hours after the end of each infusion	By Clauss and ELISA
Difference in plasma fibrinogen levels	From pre-infusion to 24 hours after the end of each infusion	By Clauss and ELISA
Incremental IVR	During the first 4 hours of sampling after the end of each infusion of FIB Grifols calculated using concentration of plasma fibrinogen	Measured by both Clauss method (functional) and ELISA method (immunologic) for subjects with acute bleeding episodes or need for additional post-operative FIB Grifols infusion

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