Phase 3 Trial of TAK-330 for Reversal of Direct Oral Factor Xa Inhibitor-induced Anticoagulation

Estado	**Tipo de Participantes**	**Rangos de Edad**
Reclutando	Sujetos incapaces de otorgar consentimiento	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase III	212
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	seguridad, eficacia	NO

Información

Identificador
2022-503012-16-00 (CTIS)

Cod. Protocolo
TAK-330-3001

Transicionado 2021-004138-12

Área terapéutica
Enfermedades [C] - Hematología [C15]|

Enfermedad investigada
Patients on treatment with Factor Xa Inhibitor needing for an urgent intervention associated with a high risk of bleeding.

Título Científico
TAK-330-3001 - A Phase 3, Prospective, Randomized, Open-label, Adaptive Group Sequential, Multicenter Trial with Blinded Endpoint Assessment to Evaluate the Efficacy and Safety of TAK-330 for the Reversal of Direct Oral Factor Xa Inhibitor-induced Anticoagulation in Patients Requiring Urgent Surgery/Invasive Procedure

Justificación

No aportado

Objetivo Principal

To evaluate intraoperative efficacy of TAK-330 in comparison with standard of care (SOC) 4F-PCC, for reversal of anticoagulation in patients receiving direct oral Factor Xa inhibitors and requiring urgent surgery/invasive procedure within 15 hours from the last dose of Factor Xa inhibitor or at any time after that if their specific DOAC calibrated (apixaban, rivaroxaban or edoxaban) anti-FXa levels were > 75ng/mL or heparin-calibrated anti FXa assay level of > 0.5 IU/mL at screening.

Variables de Evaluación Primaria

Occurrence of intraoperative effective hemostasis assessed at the end of the surgery/invasive procedure based on the assessment of the PI, the surgeon or a qualified member of the surgical team using the Four Point Intraoperative Hemostatic Efficacy Scale (Section 8.2.2.1).

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To assess the safety and postoperative efficacy of TAK 330 in comparison with SOC 4F-PCC, for reversal of anticoagulation in patients receiving direct oral Factor Xa inhibitors and requiring urgent surgery/invasive procedure within 15 hours of the last dose of Factor Xa inhibitor, or at any time after that if their specific DOAC-calibrated (apixaban, rivaroxaban or edoxaban) anti-FXa levels were > 75ng/mL, or heparin-calibrated anti-FXa assay levels of > 0.5 IU/mL at screening.

Variables de Evaluación Secundaria

Key Secondary Endpoint: Occurrence of postoperative effective hemostasis assessed at 24 hours after the end of investigational product infusion (TAK-330 or comparator 4F-PCC) based on the assessment of the PI, the surgeon or a qualified member of the surgical team using the Four Point Postoperative Hemostatic Efficacy Scale (Section 8.2.2.1).
Occurrence of intraoperative effective hemostasis assessed at the end of the surgery/invasive procedure based on the assessment of the PI, the surgeon or a qualified member of the surgical team using the Hemostatic Efficacy Rating Algorithm (Section 8.2.2.2).
Usage of blood products or non-study hemostatic agents for bleeding control within 24 hours after the end of investigational product infusion.
Number of units of packed red blood cells (PRBCs) administered to achieve bleeding control within 24 hours after the end of investigational product infusion.
Occurrence of serious adverse events (SAEs), and/or adverse events (AEs), treatment emergent AEs (TEAEs), and

adverse events of special interest (AESIs) within 30 days after the end of the surgery/invasive procedure.
Occurrence of thrombotic events within 30 days after the end of the surgery/invasive procedure.
All-cause deaths within 30 days post-surgery/invasive procedure.

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Patient or legally authorized representative willing to sign e-consent/written informed consent form (ICF). Patients 18 years of age at enrollment. Patient currently on treatment with oral Factor Xa inhibitor (rivaroxaban, apixaban, edoxaban). In the opinion of the surgeon, the patient requires urgent surgery/procedure that is associated with high-risk of intraoperative bleeding within 15 hours of the last Factor Xa inhibitor dose and requires a reversal agent for suspected direct oral Factor Xa inhibitor-related coagulopathy. In patients who are beyond the 15-hour window, eligibility requires proof of elevated plasma anti FXa levels using either specific DOAC-calibrated (apixaban, rivaroxaban or edoxaban) anti-FXa levels of > 75ng/mL, or heparin-calibrated anti-FXa assay levels of > 0.5 IU/mL at screening. Women of childbearing potential should have a negative pregnancy test documented prior to enrollment.

Criterios de Exclusión

The patient has an expected survival of less than 30 days even with best available medical and surgical care. Planned use of procoagulant drugs (e.g., Vitamin K, non-study PCCs, recombinant Factor VIIa) or blood products (transfusion of whole blood, FFP, cryoglobulins, plasma fractions, or platelets) after enrollment but before the 24±4 hours hemostatic assessment (Key secondary endpoint). Planned administration of TXA or aminocaproic acid after randomization but before the start of IP infusion, should be noted during randomization to properly stratify these patients in the IRT. Planned administration of TXA or aminocaproic acid after start of IP infusion but before the 24±4 hours hemostatic assessment is prohibited. Administration of any of the above products before the 24±4 hours hemostatic assessment will impact the assessment of hemostasis. Administration of PRBCs for hemoglobin correction, is not an exclusion criterion. Administration of unfractionated heparin within 2 hours before randomization or low molecular weight heparin within 6 hours before randomization. Hypersensitivity to PCC constituents, or any excipient of TAK-330. Patients with history of confirmed immunoglobulin A (IgA) deficiency with hypersensitivity reaction and antibodies to IgA. Septic shock as defined by persistent hypotension requiring vasopressors to maintain mean arterial pressure (MAP) 65mmHg and having blood lactate > 2 mmol despite adequate volume resuscitation. Acute or chronic liver failure (hepatic cirrhosis Child-PUGH score C). Renal failure requiring dialysis. Any other condition that could, in the opinion of the investigator, put the patient at undue risk of harm if the patient were to participate in the study. Participation in another clinical study involving an investigational product or device within 30 days prior to study enrollment, or planned participation in another clinical study involving an investigational product or device during the course of this study. Participation in an observational study is not an exclusion criterion. The use of PROTHROMPLEX TOTAL as SOC 4F-PCC. Recent history (within 90 days prior to screening) of venous thromboembolism, myocardial infarction (MI), DIC, ischemic stroke, transient ischemic attack, hospitalization for unstable angina pectoris or severe or critical coronavirus 2 (SARS-CoV-2) infection. Women who are breastfeeding at the time of enrollment. Active major bleeding defined as bleeding that requires surgery or transfusion of > 2 units of PRBC or intracranial hemorrhage with the exception of subacute and chronic subdural hemorrhages with a Glasgow Coma Score (GCS) 9. Polytrauma for which reversal of Factor Xa-inhibition alone would not be sufficient to achieve hemostasis. Known prothrombotic disorder including primary antiphospholipid syndrome, antithrombin-3 deficiency, homozygous protein C deficiency, homozygous protein S deficiency, and homozygous factor V Leiden. Known bleeding disorders (e.g., platelet function disorders, hemophilia, Von Willebrand disease, coagulation factor deficiency). Platelet count < 50,000/L. History of heparin-induced thrombocytopenia. Administration of procoagulant

drugs (e.g., non-study PCCs, recombinant Factor VIIa) or blood products (transfusion of whole blood, fresh frozen plasma (FFP), cryoglobulins, plasma fractions, or platelets) within 7 days before enrollment (Note: administration of packed red blood cells (PRBCs) for hemoglobin correction, tranexamic acid or aminocaproic acid are not exclusion criteria).

Calendario

(Última actualización: 19/02/2025)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
27/09/2022	19/12/2022	20/05/2024	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
No aportado	No aportado	No aportado	No aportado	No aportado

Promotor

Takeda Development Center Americas Inc. United States

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Contact Person

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Monetary support: N/A

Tipo de promotor: Comercial

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Centros

No iniciado (--/--/----)

Hospital Clinico Universitario De Valencia

Valencia

VALENCIA

Anesthesiology

No iniciado (--/--/----)

Hospital Universitario De Salamanca

Salamanca

SALAMANCA

Anesthesiology Deparment

No iniciado (--/--/----)

Hospital Universitario Dr Peset Aleixandre

Valencia

VALENCIA

Service of Anaesthesia and Post-Surgical Critical Care

Activo (19/12/2022)

HOSPITAL UNIVERSITARIO Y POLITECNICO LA FE

València

VALENCIA

Oncology Department

No iniciado (--/--/----)

Hospital Universitario Y Politecnico La Fe

Valencia

VALENCIA

Anesthesia Department

Medicamentos

PROTHROMPLEX TOTAL®
SOLUTION FOR INJECTION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

-
-
INTRAVENOUS USE

Código ATC: B02BD01 - FACTORES DE LA COAGULACION IX, II, VII Y X EN COMBINACION

Principios Activos: N/A

Experimental

Sin resultados

Phase 3 Trial of TAK-330 for Reversal of Direct Oral Factor Xa Inhibitor-induced Anticoagulation

State	Type of participants	Age Ranges
Recruiting	Incapable subjects of giving consent	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase III	212
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	safety, effectiveness	NO

Information

Identifier
2022-503012-16-00 (CTIS)

Protocol Code
TAK-330-3001

Transitioned 2021-004138-12

Therapeutic area
Diseases [C] - Hemic and Lymphatic Diseases [C15]|

Investigated Disease
Patients on treatment with Factor Xa Inhibitor needing for an urgent intervention associated with a high risk of bleeding.

Scientific Title
TAK-330-3001 - A Phase 3, Prospective, Randomized, Open-label, Adaptive Group Sequential, Multicenter Trial with Blinded Endpoint Assessment to Evaluate the Efficacy and Safety of TAK-330 for the Reversal of Direct Oral Factor Xa Inhibitor-induced Anticoagulation in Patients Requiring Urgent Surgery/Invasive Procedure

Rationale

Not provided

Main Objective

To evaluate intraoperative efficacy of TAK-330 in comparison with standard of care (SOC) 4F-PCC, for reversal of anticoagulation in patients receiving direct oral Factor Xa inhibitors and requiring urgent surgery/invasive procedure within 15 hours from the last dose of Factor Xa inhibitor or at any time after that if their specific DOAC calibrated (apixaban, rivaroxaban or edoxaban) anti-FXa levels were > 75ng/mL or heparin-calibrated anti FXa assay level of > 0.5 IU/mL at screening.

Primary Endpoints

Occurrence of intraoperative effective hemostasis assessed at the end of the surgery/invasive procedure based on the assessment of the PI, the surgeon or a qualified member of the surgical team using the Four Point Intraoperative Hemostatic Efficacy Scale (Section 8.2.2.1).

Temporary moments of secondary assessment

Not provided

Secondary Objective

To assess the safety and postoperative efficacy of TAK 330 in comparison with SOC 4F-PCC, for reversal of anticoagulation in patients receiving direct oral Factor Xa inhibitors and requiring urgent surgery/invasive procedure within 15 hours of the last dose of Factor Xa inhibitor, or at any time after that if their specific DOAC-calibrated (apixaban, rivaroxaban or edoxaban) anti-FXa levels were > 75ng/mL, or heparin-calibrated anti-FXa assay levels of > 0.5 IU/mL at screening.

Secondary Endpoints

Key Secondary Endpoint: Occurrence of postoperative effective hemostasis assessed at 24 hours after the end of investigational product infusion (TAK-330 or comparator 4F-PCC) based on the assessment of the PI, the surgeon or a qualified member of the surgical team using the Four Point Postoperative Hemostatic Efficacy Scale (Section 8.2.2.1).
Occurrence of intraoperative effective hemostasis assessed at the end of the surgery/invasive procedure based on the assessment of the PI, the surgeon or a qualified member of the surgical team using the Hemostatic Efficacy Rating Algorithm (Section 8.2.2.2).
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adverse events of special interest (AESIs) within 30 days after the end of the surgery/invasive procedure.
Occurrence of thrombotic events within 30 days after the end of the surgery/invasive procedure.
All-cause deaths within 30 days post-surgery/invasive procedure.

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Patient or legally authorized representative willing to sign e-consent/written informed consent form (ICF). Patients 18 years of age at enrollment. Patient currently on treatment with oral Factor Xa inhibitor (rivaroxaban, apixaban, edoxaban). In the opinion of the surgeon, the patient requires urgent surgery/procedure that is associated with high-risk of intraoperative bleeding within 15 hours of the last Factor Xa inhibitor dose and requires a reversal agent for suspected direct oral Factor Xa inhibitor-related coagulopathy. In patients who are beyond the 15-hour window, eligibility requires proof of elevated plasma anti FXa levels using either specific DOAC-calibrated (apixaban, rivaroxaban or edoxaban) anti-FXa levels of > 75ng/mL, or heparin-calibrated anti-FXa assay levels of > 0.5 IU/mL at screening. Women of childbearing potential should have a negative pregnancy test documented prior to enrollment.

Exclusion criteria

The patient has an expected survival of less than 30 days even with best available medical and surgical care. Planned use of procoagulant drugs (e.g., Vitamin K, non-study PCCs, recombinant Factor VIIa) or blood products (transfusion of whole blood, FFP, cryoglobulins, plasma fractions, or platelets) after enrollment but before the 24±4 hours hemostatic assessment (Key secondary endpoint). Planned administration of TXA or aminocaproic acid after randomization but before the start of IP infusion, should be noted during randomization to properly stratify these patients in the IRT. Planned administration of TXA or aminocaproic acid after start of IP infusion but before the 24±4 hours hemostatic assessment is prohibited. Administration of any of the above products before the 24±4 hours hemostatic assessment will impact the assessment of hemostasis. Administration of PRBCs for hemoglobin correction, is not an exclusion criterion. Administration of unfractionated heparin within 2 hours before randomization or low molecular weight heparin within 6 hours before randomization. Hypersensitivity to PCC constituents, or any excipient of TAK-330. Patients with history of confirmed immunoglobulin A (IgA) deficiency with hypersensitivity reaction and antibodies to IgA. Septic shock as defined by persistent hypotension requiring vasopressors to maintain mean arterial pressure (MAP) 65mmHg and having blood lactate > 2 mmol despite adequate volume resuscitation. Acute or chronic liver failure (hepatic cirrhosis Child-PUGH score C). Renal failure requiring dialysis. Any other condition that could, in the opinion of the investigator, put the patient at undue risk of harm if the patient were to participate in the study. Participation in another clinical study involving an investigational product or device within 30 days prior to study enrollment, or planned participation in another clinical study involving an investigational product or device during the course of this study. Participation in an observational study is not an exclusion criterion. The use of PROTHROMPLEX TOTAL as SOC 4F-PCC. Recent history (within 90 days prior to screening) of venous thromboembolism, myocardial infarction (MI), DIC, ischemic stroke, transient ischemic attack, hospitalization for unstable angina pectoris or severe or critical coronavirus 2 (SARS-CoV-2) infection. Women who are breastfeeding at the time of enrollment. Active major bleeding defined as bleeding that requires surgery or transfusion of > 2 units of PRBC or intracranial hemorrhage with the exception of subacute and chronic subdural hemorrhages with a Glasgow Coma Score (GCS) 9. Polytrauma for which reversal of Factor Xa-inhibition alone would not be sufficient to achieve hemostasis. Known prothrombotic disorder including primary antiphospholipid syndrome, antithrombin-3 deficiency, homozygous protein C deficiency, homozygous protein S deficiency, and homozygous factor V Leiden. Known bleeding disorders (e.g., platelet function disorders, hemophilia, Von Willebrand disease, coagulation factor deficiency). Platelet count < 50,000/L. History of heparin-induced thrombocytopenia. Administration of procoagulant

drugs (e.g., non-study PCCs, recombinant Factor VIIa) or blood products (transfusion of whole blood, fresh frozen plasma (FFP), cryoglobulins, plasma fractions, or platelets) within 7 days before enrollment (Note: administration of packed red blood cells (PRBCs) for hemoglobin correction, tranexamic acid or aminocaproic acid are not exclusion criteria).

Calendar

(Last Update: 19/02/2025)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
27/09/2022	19/12/2022	20/05/2024	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
Not aported	Not aported	Not aported	Not aported	Not aported

Sponsor

Takeda Development Center Americas Inc. United States

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Monetary support: N/A

Sponsor type: Commercial

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Sites

not initialized (--/--/----)

Hospital Clinico Universitario De Valencia

Valencia

VALENCIA

Anesthesiology

not initialized (--/--/----)

Hospital Universitario De Salamanca

Salamanca

SALAMANCA

Anesthesiology Deparment

not initialized (--/--/----)

Hospital Universitario Dr Peset Aleixandre

Valencia

VALENCIA

Service of Anaesthesia and Post-Surgical Critical Care

Active (19/12/2022)

HOSPITAL UNIVERSITARIO Y POLITECNICO LA FE

València

VALENCIA

Oncology Department

not initialized (--/--/----)

Hospital Universitario Y Politecnico La Fe

Valencia

VALENCIA

Anesthesia Department

Medication

PROTHROMPLEX TOTAL®
SOLUTION FOR INJECTION
INTRAVENOUS USE

-

Active Principles: N/A

Experimental

-
-
INTRAVENOUS USE

ATC code: B02BD01 - FACTORES DE LA COAGULACION IX, II, VII Y X EN COMBINACION

Active Principles: N/A

Experimental

No results