A Randomized, Placebo-Controlled, Double-Blind, Multicenter Study to Assess the Efficacy and Safety of Branebrutinib Treatment in Subjects with Active Systemic Lupus Erythematosus or Primary Sjögren's Syndrome, or Branebrutinib Treatment Followed by Open-label Abatacept Treatment in Subjects with Active Rheumatoid Arthritis.

Published: 11-02-2020
Last updated: 08-04-2024

pSS: • To compare the efficacy of branebrutinib with PBO at Week 24 in the treatment of subjects with pSS• To compare the safety and tolerability of branebrutinib with PBO in subjects with pSSRA: • To compare the efficacy of branebrutinib with PBO...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON52687

Source
ToetsingOnline

Brief title
IM014029

Condition

- Autoimmune disorders
- Joint disorders
- Skin and subcutaneous tissue disorders NEC

Synonym
and elsewhere in the body; this causes the most common symptoms of Sjögren's syndrome, lupus is called an autoimmune disease., or proteins directed against body tissue. Thus, particularly the glands that produce moisture in the eyes, pSS: Sjögren's syndrome is a chronic autoimmune disease in which the body's immune system inappropriately attacks one's own tissues, resulting in swelling and pain in and around the joints. The synovium makes a fluid that lubricates joints and helps them move smoothly. SLE: SLE develops when the body becomes allergic to itself. In lupus, the body overreacts to an unknown stimulus and makes too many antibodies, the mouth, which are dry eyes and dry mouth. RA: Rheumatoid Arthritis (RA) is an autoimmune disease in which the body□s immune system - which normally protects its health by attacking foreign substances like bacteria and viruses - overreacts and mistakenly attacks

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Bristol-Myers Squibb International Corporation

Intervention

Keyword: BRANEBRUTINIB/ABACATEPT, LUPUS, PRIMARY SJÖGREN'S SYNDROME, RHEUMATOID ARTHRITIS

Outcome measures

Primary outcome

pSS;

Proportion of subjects with at least 3 of the following at Week 24:

• Decrease of >= 1 point or 15% from baseline in the ESSPRI Total Score

• Decrease of >= 3 points from baseline in ESSDAI score

• Decrease of >= 25% from baseline in ocular staining score, or if normal score

at baseline no change to abnormal

• Increase of >= 25% from baseline in stimulated salivary flow

• Improvement in one or more serological markers (RF, IgG, complement C3 or C4, cryoglobulin)

RA:

• ACR50 response compared to baseline

SLE:

Proportion of subjects with:

>= 50% decrease in mCLASI activity score in subjects with a baseline mCLASI score >= 10

AND

CS (prednisone or equivalent) <= 10 mg at Week 20 and Week 24

Secondary outcome

RA:

• Changes in efficacy measures, including Disease Activity Score with 28 joint count and CRP or ESR [DAS28-CRP and DAS28-ESR], SDAI, and CDAI

• ACR20 and ACR70 response compared to baseline

SLE:

• Change from baseline in SLEDAI-2K score

Study description

Background summary

pSS/RA/SLE: Animal and human studies have shown that Branebrutinib was safe and well tolerated and may be useful to treat the signs and symptoms of pSS/RA/SLE. Branebrutinib is an investigational drug. Investigational means that the drug has not been approved by the regulatory authorities in the country in which the use occurs.

RA: Abatacept is a biologic compound (modified antibody) that interferes with the immune activity of T cells in the patient's blood. This drug is approved by Health Authorities (FDA and EMA) for the treatment of subjects with moderate to severe RA.

Study objective

pSS: • To compare the efficacy of branebrutinib with PBO at Week 24 in the treatment of subjects with pSS
• To compare the safety and tolerability of branebrutinib with PBO in subjects with pSS

RA: • To compare the efficacy of branebrutinib with PBO at Week 12 in the treatment of subjects with moderate to severe RA on a stable background of MTX who have had an inadequate response to MTX
• To evaluate the efficacy at Week 24 of switching from branebrutinib or PBO to abatacept at Week 12 in the treatment of subjects with moderate to severe RA

SLE: • To compare the efficacy of branebrutinib with PBO at Week 24 in the treatment of subjects with SLE
• To compare the safety and tolerability of branebrutinib with PBO in subjects with SLE

Study design

pSS: • This is a double-blind, PBO-controlled Phase 2a study sub-protocol to evaluate the effect of branebrutinib (BMS 986195) in subjects with pSS. All subjects will receive background therapy for their primary disease as appropriate.
• Subjects will receive double-blind oral (PO) branebrutinib 9 mg or PBO treatment once daily for 24 weeks (Week 0 to Week 24).
• Treatment assignment will be conducted by randomization. Subjects will

undergo screening evaluations to determine eligibility within 28 days prior to administration of study medication. Following the screening process, if eligible for study participation, subjects will be randomized to receive branebrutinib or PBO treatment in a 2:1 ratio. Randomization will be stratified by hydroxychloroquine (HCQ) use (yes/no).

RA: • This is a double-blind, PBO-controlled Phase 2a study sub-protocol to evaluate the effect of branebrutinib (BMS 986195) in subjects with RA. All subjects will receive background therapy for their primary disease as appropriate.
• Subjects will receive double-blind branebrutinib 9 mg administered orally (PO) once daily (QD) or branebrutinib PBO for 12 weeks (Week 0 to Week 12). Note: the last day of dosing of branebrutinib or PBO in the RA sub-protocol should be the day prior to the Week 12/Day 85 visit.
• All subjects will receive an additional 12 weeks of treatment (Week 12 to Week 24) with open-label abatacept.
• Treatment assignment will be randomized. Subjects will undergo screening evaluations to determine eligibility within 28 days prior to administration of study medication. Following the screening process, if eligible for study participation, subjects will be randomized in the study to the RA sub-protocol in a 3:1 ratio for study treatment and PBO. No stratification will be imposed at randomization in this sub-protocol.

SLE: • This is a double-blind, PBO-controlled Phase 2a sub-protocol to evaluate the effect of branebrutinib (BMS-986195) in subjects with active SLE. All subjects will continue background therapy for their primary disease within protocol-defined limits.
• Subjects will receive double-blind branebrutinib 9 mg or PBO treatment administered orally (PO) once daily (QD) for 24 weeks (Week 0 to Week 24).
• Treatment assignment will be conducted by randomization. Subjects will undergo screening evaluations to determine eligibility within 28 days prior to administration of study medication. Following the screening process, if eligible for study participation, subjects will be randomized in the SLE sub-protocol to receive branebrutinib or PBO treatment in a 3:1 ratio. Randomization will be stratified by immunosuppressant use (yes/no).

Intervention

pSS Sub-protocol Duration:
The total duration of participation in the pSS sub-protocol is approximately 32 weeks and will be divided into the following periods: screening (up to 4 weeks), double-blind PBO-controlled treatment for 24 weeks (Week 0 to Week 24), and follow-up (4 weeks).

Treatment Period (V2 to V9)

We will treat the patient with study medicines for 24 weeks. Neither the patient nor the investigator will know which group the patient is in. This can be found out if important for the patient's health.
During the treatment period the patient will be asked to come back for the further visits and will have some further procedures and tests (including taking blood and urine samples).

Visits and tests
This study requires that the patient will visit the hospital 8 times over a period of 24 weeks. A visit will take approximately 2-7 hours depending on activities scheduled. Many of the tests completed during the Screening will be repeated during the Treatment period.

RA Sub-protocol Duration:
The total duration of participation in the RA sub-protocol is approximately 32 weeks and will be divided into the following periods: screening (up to 4 weeks), double-blind, PBO-controlled branebrutinib treatment for 12 weeks (Week 0 to Week 12), open-label treatment with abatacept for an additional 12 weeks (Week 12 to Week 24), and follow-up (4 weeks).

Treatment Period (V2 to V10)
We will treat the patient with study medicines for 24 weeks.
There are 9 visits during the treatment period and many of the screening tests will be repeated. The first treatment visit is visit 2. Each visit will last approximately 2-7 h depending on the activities scheduled .Neither the patient nor the investigator will know which group the patient is in. This can be found out if important for the patient's health.

Visits and tests
This study requires that the patient will visit the hospital 9 times over a period of 24 weeks. A visit will take approximately 2-7 hours depending on activities scheduled.

SLE Sub-protocol Duration:
The total duration of participation in the SLE sub-protocol is approximately 32 weeks and will be divided into the following periods: screening (up to 4 weeks), double-blind PBO-controlled treatment for 24 weeks (Week 0 to Week 24), and follow-up (4 weeks).

Treatment Period (V2 to V10)
We will treat the patient with study medicines for 24 weeks. Neither the patient nor the investigator will know which group the patient is in. This can

be found out if important for the patient's health.
During the treatment period the patient will be asked to come back for the further visits and will have some further procedures and tests (including taking blood and urine samples).

Visits and tests
This study requires that the patient will visit the [hospital 8 times over a period of 24 weeks. A visit will take approximately 2-7 hours depending on activities scheduled. Many of the tests completed during the Screening will be repeated during the Treatment period.

Study burden and risks

Participation in the study also means:
- additional time;
- additional or longer hospital stays;
- additional tests;
- instructions the patient needs to follow.

risks pSS:
Some procedures that will be done during the study may carry some risks, these are given below, and the study doctor can provide more information to the patient.

Blood Sample
Blood samples will be collected during this study. A needle is inserted into a vein in the patient's arm and a small blood sample is withdrawn. Although one needle insertion for blood draw is usually sufficient, a second one may be necessary if the first is not successful. Collecting blood samples may cause fainting and some pain and/or bruising at the site on the patient's arm where the blood was taken. In rare occasions, infection may occur.

ECG
ECG will be performed, which is a process of recording the electrical activity of the heart over a short period of time using sticky pads placed on the skin to measure the rate and rhythm of the patient's heartbeats. The sticky pads may cause mild skin irritation.

X-ray
The patient may receive an X-ray as part of the study. An X-ray is a form of radiation. The radiation the patient receives from the X-ray is minimal. However, the more radiation the patient receives over the course of life increases the risk of cell changes in the body or having cancerous tumors. The radiation from this study is not expected to greatly increase these risks, but the exact increase of such risks is unknown.

Fasting Blood Sample
The patient will be asked to fast for 8-10 hours prior to some study visits which may cause dizziness, low blood sugar and in rare occasions, fainting.

Collection of saliva for stimulated salivary flow
The patient may experience nausea while chewing to stimulate saliva production.

Eye assessments for dryness
The patient may experience some discomfort or irritation during the Schirmer*s test while the paper strips are resting in the eyelids. The patient may also experience some mild eye irritation from the dyes that are used for the ocular surface staining and tear break-up time tests. The patient may have some residual staining (depending on the dye used) of the eyes for a few hours after these procedures. Lastly, the bright light used in the slit lamp to examine the patient's eyes may cause some discomfort.
*
Biopsy (for optional sub study only)
If the patient accepts to take part on the optional sub study, the patient will be requested for a labial salivary gland or parotid gland biopsy. There is a risk of some pain, discomfort or infection associated to this procedure, since an incision in the mucosa of the lower lip through the epithelium is performed. Bleeding, bruising or swelling could also occur.

Lip salivary biopsy: the patient may experience some soreness at the site of the lip salivary gland biopsy for a few days after the procedure. A small percentage of participants may also experience numbness at the site of the biopsy, and in rare cases the numbness may be permanent. A small scar may form at the site which may also remain numb.
Parotid gland biopsy: the patient may experience some soreness at the site of the incision and some temporary numbness at the site. A small scar may form at the incision site.

General care measures are recommended as standard treatment for subjects with pSS, unless otherwise informed by the patient's doctor, e.g. to treat a side effect. These general care measures include: use of artificial tears (eye drops) for dry eyes, stimulating saliva by sucking on sugarless candy to improve dry mouth, preventing cavities by brushing and flossing after eating meals, use petroleum for dry lips, frequent and liberal use of a moisturizing cream or ointment to improve dry skin or the use of vaginal moisturizers or estrogen cream to treat vaginal dryness, especially after menopause and other similar measures.

There may be risks or side effects related to the study drug or other study procedures that are unknown at this time. Let the study doctor know if the patient experiences any side effects, even those which are not mentioned in this Information sheet. The study doctor will inform the patient (or the

legally authorized representative) if new information on the study medication becomes available that may affect the patient's decision to continue to take part in the study

RA risks:
Some procedures that will be done during the study may carry some risks, these are given below, and the patient's study doctor can provide more information to the patient.

Blood Sample
Blood samples will be collected during this study. A needle is inserted into a vein in the patient's arm and a small blood sample is withdrawn. Although one needle insertion for blood draw is usually sufficient, a second one may be necessary if the first is not successful. Collecting blood samples may cause fainting and some pain and/or bruising at the site on the patient's arm where the blood was taken. In rare occasions, infection may occur.

ECG
ECG will be performed, which is a process of recording the electrical activity of the heart over a short period of time using sticky pads placed on the skin to measure the rate and rhythm of the patient's heartbeats. The sticky pads may cause mild skin irritation.

MRI Scan with gadolinium contrast
MRI is a non-invasive (not entering or penetrating the body or body tissue) imaging test that uses a magnetic field and pulses of radio wave energy to take pictures of organs and structures inside the body. The patient will need to lay flat in a special machine that contains a magnet. People who are claustrophobic (feel uncomfortable in confined spaces) may feel uncomfortable inside the MRI machine. If the patient feels uncomfortable in confined spaces, please tell the study doctor. The patient can request that the MRI be stopped at any time, but the scan may not be complete.
As part of the MRI scan, the patient will receive an intravenous injection of gadolinium, a contrast agent. This injection increases the accuracy of the scan. Gadolinium contrast has been used safely in many cases, but minor reactions such as headache, nausea, or itchiness occur in about 2% of subjects, and very rare severe reactions, including severe allergic reactions occur in less than one in 40,000 subjects. The patient will be monitored for any signs or symptoms of gadolinium reaction.

X-ray
The patient may receive an X-ray as part of the study. An X-ray is a form of radiation. The radiation the patient receives from the X-ray is minimal. However, the more radiation the patient receives over the course of life increases the risk of cell changes in the body or having cancerous tumors. The

radiation from this study is not expected to greatly increase these risks, but the exact increase of such risks is unknown.

Fasting Blood Sample
The patient will be asked to fast for 8-10 hours prior to some study visits which may cause dizziness, low blood sugar and in rare occasions, fainting.

Injection site reactions with abatacept The patient may experience pain, redness, swelling, itching or bruising at the site of the study drug injection.

SLE risks:

Blood Sample
Blood samples will be collected during this study. A needle is inserted into a vein in the patient's arm and a small blood sample is withdrawn. Although one needle insertion for blood draw is usually sufficient, a second one may be necessary if the first is not successful. Collecting blood samples may cause fainting and some pain and/or bruising at the site on the patient's arm where the blood was taken. In rare occasions, infection may occur.

ECG
ECG will be performed, which is a process of recording the electrical activity of the heart over a short period of time using sticky pads placed on the skin to measure the rate and rhythm of the patient's heartbeats. The sticky pads may cause mild skin irritation.

X-ray
The patient may receive an X-ray as part of the study. An X-ray is a form of radiation. The radiation the patient receives from the X-ray is minimal. However, the more radiation the patient receives over the course of life increases the risk of cell changes in the body or having cancerous tumors. The radiation from this study is not expected to greatly increase these risks, but the exact increase of such risks is unknown.

Fasting Blood Sample
The patient will be asked to fast for 8-10 hours prior to some study visits which may cause dizziness, low blood sugar and in rare occasions, fainting.

General skin care measures are recommended that are standard for participants with SLE, unless otherwise informed by the patient's doctor, e.g. to treat a side effect. These general skin care measures include: use of broad spectrum sunscreen (minimum sun protection factor 15 and with inorganic ingredients (zinc oxide, titanium dioxide), avoiding sun exposure, wearing sun-protective clothing, avoidance of alcohol-based emollients, avoidance of over-the-counter anti-acne medications and alcohol-based skin care products, and avoidance of

perfumed soaps and detergents, and similar measures.

There may be risks or side effects related to the study drug or other study procedures that are unknown at this time. Let the study doctor know if the patient experiences any side effects, even those which are not mentioned in this Information sheet. The study doctor will inform the patient (or legally authorized representative) if new information on the study medication becomes available that may affect the patient's decision to continue to take part in the study.

Contacts

Public
Bristol-Myers Squibb

Chaussée de la Hulpe 185
Brussels 1170
BE
Scientific
Bristol-Myers Squibb

Chaussée de la Hulpe 185
Brussels 1170
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Sub-Protocol for Systemic Lupus Erythematosus (SLE):

- Active SLE as defined by the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) classification.
- Diagnosed with SLE more than 24 weeks before screening visit.
Sub-Protocol for primary Sjögren's Syndrome (pSS):
- Moderate to severe pSS, meeting ACR-EULAR classification criteria.
Sub-Protocol for active Rheumatoid Arthritis (RA):
- Moderate to severe adult-onset RA.
- ACR global functional status class I to III.
For all sub-studies:
- Women and men must agree to follow instructions for methods of contraception.
Please, be referred to the Protocol document for a complete list of Inclusion citeria.

Exclusion criteria

Sub-Protocol for Systemic Lupus Erythematosus (SLE):
- Certain other autoimmune diseases and overlap syndromes.
Sub-Protocol for primary Sjögren's Syndrome (pSS):
- Certain other immune-mediated diseases, active fibromyalgia, or other medical conditions.
Sub-Protocol for Rheumatoid Arthritis (RA):
- Diagnosis with juvenile arthritis or idiopathic arthritis before age 16.
For all sub-studies:
- History of any significant drug allergy
- Active infection, significant concurrent medical condition, or clinically significant abnormalities
Please, be referred to the Protocol document for a complete list of Exclusion citeria.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-01-2020
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Abatacept
Generic name:	Orencia
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Branebrutinib
Generic name:	not applicable

Ethics review

Approved WMO Date:	11-02-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-06-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-09-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	17-03-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-05-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-07-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-09-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	142401 (IND)
EudraCT	EUCTR2019-002205-22-NL

Register	ID
CCMO	NL72072.042.20