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A study of VAC85135, a neoantigen vaccine regimen, concurrently administered with ipilimumab for the treatment of myeloproliferative neoplasms

Submission date
17/02/2023

Recruitment status
No longer recruiting

Registration date
28/02/2023

Overall study status
Completed

Last Edited
26/10/2026

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Myeloproliferative neoplasms (MPNs) are a group of blood cancers in which the bone marrow makes too many red/white blood cells or platelets or develops scarring that prevents the production of normal cells. MPNs are rare, and the most common types are essential thrombocythemia (ET), polycythemia vera (PV), and primary myelofibrosis (PMF). Due to limited treatment options available, new effective therapies are needed. One approach is a vaccine to train the immune system to reduce the growth of cancer cells and improve the quality of life of patients with these diseases. VAC85135 is a combination vaccine, with two distinct forms, that uses two different viruses carrying genetic material encoding protein fragments only expressed in cancer cells. The goal of the vaccine is to train the immune system to attack the cancer cells that express these abnormal proteins. The study is designed to see if VAC85135 can be safely administered to adult participants with MPNs in combination with ipilimumab.

Who can participate?
Adult patients aged 18 years and over with MPNs

What does the study involve?
This is the first study of VAC85135 in humans. It involves a screening period (≤30 days before treatment) followed by a treatment period (≤30 days after the last dose of VAC85135).
The treatment period consists of 2 parts:
Part 1 (Dose Escalation): All participants receive the same dose of VAC85135, and different dose levels of ipilimumab will be tested. The different ipilimumab doses are tested to study the safety of each dose.
Part 2 (Dose Expansion): Participants will receive VAC85135 at the same dose in addition to the dose of ipilimumab determined during Part 1.
After discontinuation of treatment, participants will be monitored for up to 12 weeks.

During the study, some tests will be performed including blood tests, vital signs, bone marrow tests, ECOG, and pregnancy tests. Blood samples will be taken at multiple timepoints to understand how the body responds to treatment. All side effects will be recorded till the study ends (1 year and 5 months).

What are the possible benefits and risks of participating?
Participants may not receive any benefit from taking part in this study, but the information that is learned from the study may help develop treatments for people with MPNs in the future.
This is a first-in-human study which means that VAC85135 has not been given to people before. The possible risks for VAC85135, based on how the drug works and results from laboratory studies are listed below:
• Allergic reactions
• Syncope (loss of consciousness due to insufficient blood flow to the brain)
• Injection site reactions
• Immune-mediated adverse reactions
• Thrombosis with thrombocytopenia (blood clots with low platelets count)
• Guillain-Barré syndrome (the body's immune system attacks nerves)
The participant information sheet and informed consent form, which will be signed by every participant agreeing to take part in the study, includes a detailed section outlining the risks of participating in the study. Participants may have none, some, or all of the possible side effects listed, and they may be mild, moderate, or severe. To minimise the risk associated with taking part, participants are frequently reviewed for any side effects and other medical events. If they have any side effects or are worried about them, or have any new or unusual symptoms, participants will be encouraged to talk with their study doctor. The study doctor will also be looking out for side effects and will provide appropriate medical care. There may also be side effects that the researchers do not expect or do not know about and that may be serious. Many side effects go away shortly after the intervention ends. However, sometimes side effects can be serious, long-lasting, or permanent. If a severe side effect or reaction occurs, the study doctor may need to stop the procedure. The study doctor will discuss the best way of managing any side effects with participants. There is always a chance that an unexpected or serious side effect may happen. This can happen to people who take this or any other drug.

Where is the study run from?
The study is run across multiple medical facilities located in the United Kingdom, France, Canada, the United States of America and Spain.

When is the study starting and how long is it expected to run for?
May 2022 to February 2026

Who is funding the study?
Janssen Research & Development, LLC (Belgium)

Who is the main contact?
Ms Florence Baluwa, Janssen Research and Development, JanssenUKRegistryQueries@its.jnj.com (UK)

Contact information

Type(s)
Public

Contact name
Ms Florence Baluwa

Contact details
Janssen Research & Development (Janssen-Cilag Ltd), 20 Grenfell Road
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Type(s)
Scientific

Contact name
None Medical Information and Product Information Enquiry

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+44 (0)800 731 8540, (0)1494 567 444
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Type(s)
Principal investigator

Contact name
Prof Claire Harrison

Contact details
Guys St Thomas NHS Foundation Trust
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United Kingdom
None provided

Additional identifiers

ClinicalTrials.gov (NCT)
NCT05444530

Clinical Trials Information System (CTIS)
2021-006033-20

Integrated Research Application System (IRAS)
1005965

Central Portfolio Management System (CPMS)
53963

Protocol serial number
VAC85135MPN1001

Study information

Scientific Title
A phase I study of VAC85135, a neoantigen vaccine regimen, concurrently administered with ipilimumab for the treatment of myeloproliferative neoplasms

Study objectives
To evaluate the safety of VAC85135 administered with ipilimumab for the treatment of MPNs.
To evaluate the immunogenicity of VAC85135 administered with ipilimumab for the treatment of MPNs
To evaluate preliminary anti-tumor clinical activity of VAC85135administered with ipilimumab for the treatment of MPNs

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/01/2023, South Central - Oxford A Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44 (0)207 1048171, (0)207 1048206, (0) 207 1048276; oxforda.rec@hra.nhs.uk), ref: 22/SC/0427

Primary study design
Interventional

Study design
Interventional phase I sequential-assignment no-masking non-randomized study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Myeloproliferative neoplasms

Interventions
Part 1: Dose Escalation; Participants with essential thrombocythemia (ET) and myelofibrosis (MF) will receive VAC85135 target dose intramuscular (IM) injection in the safety lead-in cohort (Cohort 0). Participants in subsequent cohorts will receive VAC85135 target dose IM injection along with ipilimumab intravenous (IV) infusion. Ipilimumab dose may be escalated based on dose

Part 2: Dose Expansion; Participants with polycythemia vera (PV) or post-polycythemia vera myelofibrosis, ET and MF will receive VAC85135 target dose IM injection with ipilimumab IV infusion at the dose(s) determined by study evaluation team (SET).

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
VAC85135, ipilimumab

Primary outcome(s)
Current primary outcome measure as of 16/02/2024:

1. Number of participants with dose-limiting toxicity (DLT), defined as any of the following: high-grade non-hematologic toxicity, or hematologic toxicity, measured according to the National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 5.0 from Baseline (Day 1) up to Day 78
2. Number of participants with adverse events (AEs) and serious adverse events (SAEs), defined as any untoward medical occurrence in a clinical study participant administered a pharmaceutical product, measured using study patient records up to 79 weeks. AEs will be graded as Grade 1: Mild- asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated; Grade 2: Moderate- minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL); Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living; Grade 4- Life-threatening consequences- urgent intervention indicated; Grade 5: Death related to AE.

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Previous primary outcome measure:

1. Number of participants with dose-limiting toxicity (DLT), defined as any of the following: high-grade non-hematologic toxicity, or hematologic toxicity, measured according to the National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 5.0 from Baseline (Day 1) up to Day 78
2. Number of participants with adverse events (AEs) and serious adverse events (SAEs), defined as any untoward medical occurrence in a clinical study participant administered a pharmaceutical product, measured using study patient records up to 76 weeks. AEs will be graded as Grade 1: Mild- asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated; Grade 2: Moderate- minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL); Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living; Grade 4- Life-threatening consequences- urgent intervention indicated; Grade 5: Death related to AE.

Key secondary outcome(s)
Current secondary outcome measures as of 16/02/2024:

1. Number of participants with antigen-specific T-cell response measured using Elispot up to end of treatment (EOT) (up to 64 weeks)
2. Number of participants with overall response measured by complete remission, partial remission, clinical improvement, anemia response, spleen response, symptoms response, progressive disease, stable disease and relapse as per the revised response criteria by the International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) Consensus Report response criteria for myelofibrosis (MF) up

to 79 weeks
3. Number of participants with a disease response measured per Modified IWG-MRT Criteria at weeks 24, 48 and EOT
4. Number of participants with peripheral blood mutant calreticulin (mutCALR) and janus kinase 2 with V617F mutation (JAK2V617F) allele burden measured using peripheral blood sample analysis up to end of treatment (EOT) (Up to 64 weeks)
5. Number of participants with transfusion burden measured using the number of transfusions participants received, each transfusion received will be recorded, up to EOT at 64 weeks
6. Number of participants with patient-reported symptoms on therapy measured using a Total Symptom Score on Patient-reported Outcomes (PROs) questionnaire up to EOT at 64 weeks
7. Time to progression of myeloproliferative neoplasms (MPNs; polycythemiavera [PV], essential thrombocythemia [ET], and primary myelofibrosis [PMF]) measured using the IWG-MRT and ELN consensus report up to EOT at 64 weeks

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7. Time to progression of myeloproliferative neoplasms (MPNs; polycythemiavera [PV], essential thrombocythemia [ET], and primary myelofibrosis [PMF]) measured using the IWG-MRT and ELN consensus report up to EOT at 64 weeks

Completion date
02/02/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 16/02/2024:

1. Be positive for a CALR (calreticulin) mutation: Type 1 or Type 2; Type 1-like, or Type 2-like may be considered with Sponsor approval; or positive for the JAK2V617F (Janus kinase 2 with valine 617 to phenylalanine mutation) mutation with HLA-A02:01 (human leukocyte antigens) per medical history or local testing.

2. Have an Eastern Cooperative Oncology Group (ECOG) performance status grade of 0 or 1 or 2
3. Have the following hematologic laboratory values: Leukocytes greater than or equal to (>=) 1.5 *10^9 per liter, Neutrophils >=1.0*10^9 per liter, Platelets >=20*10^9 per liter, Hemoglobin greater than (>) 7 gram per deciliter (g/dL)
4. Have the following chemistry laboratory values: Alanine aminotransferase (ALT): less than or equal to (<=) 3*upper limit of normal (ULN), aspartate aminotransferase (AST): <=3*ULN, total bilirubin: <=1.5*ULN, and glomerular filtration rate >=40 milliliter per minute (mL/min)
5. A female participant of childbearing potential must agree to all the following during the study and for 6 months after the last dose of study treatment: use a barrier method of contraception, use a highly effective preferably user-independent method of contraception, not donate eggs (ova, oocytes) or freeze for future use for the purposes of assisted reproduction, not plan to become pregnant, not to breast-feed
6. A male participant must agree to all the following during the study and for 90 days after the last dose of study treatment: wear a condom when engaging in any activity that allows for the passage of ejaculate to another person, not to father a child, not to donate sperm or freeze for future use for the purpose of reproduction

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Previous inclusion criteria:

1. Have an Eastern Cooperative Oncology Group (ECOG) performance status grade of 0 or 1 or 2
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Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment

Key exclusion criteria
Current exclusion criteria as of 16/02/2024:

1. History of any significant medical condition per investigators judgment (example: severe asthma/chronic obstructive pulmonary disease (COPD), poorly regulated heart condition, insulin-dependent diabetes mellitus)
2. Serious known clinically relevant allergies or earlier anaphylactic reactions
3. Currently pregnant or breastfeeding
4. Prior treatment with any Janus kinase 1/2 (JAK 1/2) inhibitor
5. Known sensitivity or contraindications to the use of Ipilimumab per local prescribing information

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Previous exclusion criteria:

1. History of any significant medical condition per investigators judgment (example: severe asthma/chronic obstructive pulmonary disease (COPD), poorly regulated heart condition, insulin-dependent diabetes mellitus)
2. Serious known clinically relevant allergies or earlier anaphylactic reactions
3. Currently pregnant or breastfeeding
4. Prior treatment with any Janus kinase 2 (JAK2) inhibitor
5. Known sensitivity or contraindications to the use of Ipilimumab per local prescribing information

Date of first enrolment
21/07/2022

Date of final enrolment
24/04/2024

Locations

Countries of recruitment
United Kingdom

Canada

France

Spain

United States of America

Study participating centre
Guy's and St Thomas' Hospital
Dept Of Hematology

Great Maze Pond
4th floor
Southwark Wing
London
England
SE1 9RT

Study participating centre
The Christie NHS Foundation Trust
Wilmslow Road
Manchester
England
M20 4BX

Study participating centre
Churchill Hospital
Churchill Hospital
Old Road
Headington
Oxford
England
OX3 7LE

Study participating centre
University Health Network (UHN) Princess Margaret Cancer Centre
610 University Avenue
Toronto
Canada
M5G 2C1

Study participating centre
Hospital Universitario de Salamanca
Salamanca
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37007

Study participating centre
Hospital Clinico Universitario De Valencia
Av. de Blasco Ibanez

Valencia
Spain
46010

Study participating centre
City of Hope
1500 E Duarte Road
Duarte
United States of America
91010

Study participating centre
MD Anderson Cancer Centre
1515 Holcomber Blvd
Houston, Texas
United States of America
77030

Study participating centre
Moffitt Cancer Centre
12902 USF Magnolia Drive
Tampa
Florida
United States of America
33612

Study participating centre
Cleveland Clinic
9500 Euclid Ave
Cleveland
Ohio
United States of America
44195

Sponsor information

Organisation
Janssen Research & Development, LLC

Funder(s)

Funder type
Industry

Funder Name
Janssen Research and Development

Alternative Name(s)
Janssen R&D, Janssen Research & Development, Janssen Research & Development, LLC, Janssen Research & Development LLC, Janssen Pharmaceutical Companies of Johnson & Johnson, Research & Development at Janssen, JRD, J&J PRD

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing policy of the Janssen Pharmaceutical Companies of Johnson & Johnson is available at www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site atyoda.yale.edu

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No