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A study to test mirvetuximab soravtansine in women with platinum sensitive, advanced epithelial ovarian, primary peritoneal, or fallopian tube cancers.

Submission date
24/06/2022

Recruitment status
No longer recruiting

Registration date
21/09/2022

Overall study status
Completed

Last Edited
03/10/2022

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
MIRV (study drug) is being developed by ImmunoGen, Inc. as a potential treatment for high grade ovarian, peritoneal and fallopian tube cancers. This study involve patients in which cancer has come back after treatment and tumour has tested positive for high levels of a tumour-associated protein called folate receptor alpha (FRα). The study involves pre-screening of patients to test the FRα in tumor tissue as MIRV mainly targets the FRα. The study will look at the following:
• If the study drug works (called efficacy)
• what the study drug does to the body (called pharmacodynamics).
Researchers hope MIRV will cause the cancer cells to stop growing and spreading. This drug is designed to selectively kill tumours. The antibody (protein) part of MIRV targets tumours by delivering a cell-killing drug to the tumour cells carrying FRα.
About 75 people and about 75 study sites are expected to participate in this study worldwide.

Who can participate?
Women aged 18 years or above, with confirmed diagnosis of high-grade serous EOC, primary peritoneal cancer, or fallopian tube cancer.

What does the study involve?
Patients will undergo physical exams, vital signs, blood/ urine sampling, heart examinations, eye examinations and other assessments. MIRV will be given by needle into one of the veins. This is called infusion which may take 15 minutes to 4 hours depending on the drug dose. Participants will receive infusions every 3 weeks. They can stay on the study as long as you will be doing well, and their cancer will not get worse. The total duration of participation for an individual participant is approximately 30 months including follow ups.

What are the possible benefits and risks of participating?
Benefits:

Not provided at time of registration
Risks:
MIRV is an experimental drug; therefore, the risks to human participants have not been fully evaluated. In earlier clinical trials of MIRV, the most common side effects (10% or more of patients treated with MIRV have experienced at least one of these side effects) were
• Blurred vision
• Changes in blood tests that indicate liver damage*
• Changes in the cornea– The cornea is the eye's outermost layer, which is clear, dome shaped and covers the front of the eye. Patients have experienced cloudiness, inflammation, irritation, or the formation of small cysts in the cells of the cornea. These events have been reversible.
• Diarrhoea*
• Fatigue*
• Nausea*
• Neuropathy (nerve pain) - neuropathy (numbness, tingling, or weakness in hands or feet, which is sometimes painful) has been reported.
• Vomiting (throwing-up) *
• Joint and muscle pain
• Constipation*
(The above symptoms were mild to moderate in severity, but occasionally severe events have been reported)
• Decreased appetite*
• Decreased platelets (cells that help your blood clot) * --in some cases, a need for platelet transfusion has been required. Decreased platelets may cause to bleed or bruise.
• Dry Eye - Symptoms may include stinging or burning of the eye, sandy or gritty feeling in the eye, eye pain, redness, blurred vision, inability to cry, and eye fatigue.
• Abnormal electrolytes * - this includes potassium, sodium among others. Abnormal electrolyte results, if severe, can cause muscle cramping, nausea or, in very severe cases, can affect your heart function.
• Headache*
(The above symptoms were mild to moderate in severity)
More than 1% and up to 10% of patients treated with MIRV have experienced at least one of the following symptoms, mild to moderate in severity:
• Decreased white blood cells*- Decreases in certain types of white blood cells can increase your risk of developing infection.
• Eye Irritation or eye pain
• Infusion allergic-like reaction. Symptoms can include hives, cold sweats, retching, fever, nausea, and/or headache, dizziness, or fainting (low blood pressure), flushing, rash, shortness of breath at the time of receiving your infusion (IV) or just after, or pain at the site of the infusion.
• Pneumonitis (inflammation of the lungs or lung tissues)*– patients have experienced fatigue, shortness of breath, cough, or respiratory distress. Pneumonitis may be immediately life threatening
• Dehydration*- Symptoms can include: increased thirst, dry mouth and skin, decreased urine output, dizziness, or drowsiness.
• Decreased number of red blood cells (cells that carry oxygen) Decreased red blood cells may cause you to feel tired or short of breath (mild to moderate in severity but occasionally, sever events have been reported).
*Patients have been hospitalized due to side effects.

Other Risks: The needle used to give this drug, or for blood collection, may cause swelling, bruising, or infection at the puncture sites. In rare cases during an intravenous (IV) infusion, the drug may leak out of the vein and under the skin, where it may damage the tissue and scarring. Sticky pads used for ECG may sometimes cause some discomfort such as redness or itching.

Continuous use of corticosteroid eye drops may result in infection, increased eye pressure or clouding of lens.
CT scan could cause cell damage, it is small risk and considered negligible. you may have more CT scans than you would normally have for your treatment.
MRI makes loud banging noises and could cause discomfort. It should not be performed with pacemaker or any other metal object in body.
The risk of MIVR to unborn child or to sperm is unknown. Please refer to study investigator for full list of potential risks.

Where is the study run from?
Immunogen Biopharma (Ireland) Limited

When is the study starting and how long is it expected to run for?
June 2022 to June 2024

Who is funding the study?
Immunogen Biopharma (Ireland) Limited

Who is the main contact?
Dr Sarah Ayres, sarah.ayers@pbh-tr.nhs.uk

Contact information

Type(s)
Principal investigator

Contact name
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05041257

Clinical Trials Information System (CTIS)
2021-003592-34

Integrated Research Application System (IRAS)
1005290

Central Portfolio Management System (CPMS)
52122

Protocol serial number
IMGN853-0419

Study information

Scientific Title
PICCOLO: a phase 2, single arm study of mirvetuximab soravtansine in recurrent platinum-sensitive, high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high folate receptor-alpha expression

Acronym
PICCOLO

Study objectives
Primary objectives:
To determine the efficacy of MIRV in patients with recurrent platinum-sensitive ovarian cancer (rPSOC) and high folate receptor alpha (FRα) expression.
Secondary objectives:
To determine the durability of response to MIRV in patients with rPSOC and high FRα expression.
To evaluate the safety and tolerability of MIRVTo characterize the clinical activity of MIRV in patients with rPSOC and high FRα expression.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, NRES Committee London – Westminster (80 London Road, London, SE1 6LH, United Kingdom; +44 207 1048236; westminster.rec@hra.nhs.uk), ref: 22/EM/0155

Primary study design
Interventional

Study design
Interventional non randomized trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Recurrent Platinum-Sensitive, High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancers with High Folate Receptor-Alpha Expression

Interventions
Participants will have had at least 2 prior lines of therapy. These will include at least 2 lines of platinum-containing therapy or 1 line with a documented platinum allergy. All participants will be, in the opinion of the Investigator, appropriate for non-platinum single-agent therapy for their next line of therapy.

All participants will receive single-agent Mirvetuximab Soravtansine (MIRV) at 6 mg/kg adjusted ideal body weight, administered through intravenous (IV) infusion once every 3 weeks, which is referred to as a cycle. A cycle is the length of the treatment plus rest time between treatments.

Participants will continue to receive MIRV until progress disease (PD), unacceptable toxicity, withdrawal of consent, death, or until the Sponsor terminates the study (whichever comes first).

There is a 3 month follow up, the study doctor will contact the participant every 12 weeks to collect information about how they are doing and any anticancer treatments they are receiving. There may be additional times during the study when the participant will be contacted for this information. If the participant returns to the research site for a follow up visit, a blood sample will be taken.

If the participant discontinues MIRV for reasons other than the cancer worsening, they will have a CT/MRI and blood test to assess the cancer every 6-12 weeks until either the cancer worsens, or they begin a new anticancer therapy.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
mirvetuximab soravtansine

Primary outcome(s)
Objective response rate (ORR), which includes confirmed best response of complete response (CR) or partial response (PR) as assessed by the Investigator at day 1 of every 3-week cycle (Q3W)

Key secondary outcome(s)
Measured at day 1 of every 3-week cycle (Q3W):
1. Duration of response (DOR), defined as the time from initial Investigator-assessed response (CR or PR) until progressive disease (PD) as assessed by the Investigator
2. Treatment-emergent adverse events (TEAEs) and laboratory test results, physical examination, or vital signs
3. CA-125 response determined using the Gynecologic Cancer Intergroup (GCIG) criteria
4. Progression-free survival (PFS), defined as the time from first dose of MIRV until Investigator-assessed radiological PD or death, whichever occurs first
5. Overall survival (OS), defined as the time from first dose of MIRV until death
6. ORR, DOR, and PFS by blinded independent central review (BICR) will be summarized as sensitivity analysis

Completion date
30/06/2024

Eligibility

Key inclusion criteria
1. Patients ≥18 years of age
2. Patients must have an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of

0 or 1
3. Patients must have a confirmed diagnosis of high-grade serous EOC, primary peritoneal cancer, or fallopian tube cancer
4. Patients must have platinum-sensitive disease defined as radiographic progression greater than 6 months from last dose of most recent platinum therapy
Note: Progression should be calculated from the date of the last administered dose of platinum therapy to the date of the radiographic imaging showing progression
5. Patients must have progressed radiographically on or after their most recent line of anticancer therapy
6. Patients must have at least 1 lesion that meets the definition of measurable disease by RECIST v1.1 (radiologically measured by the Investigator)
7. Patients must be willing to provide an archival tumor tissue block or slides, or undergo procedure to obtain a new biopsy using a low-risk, medically routine procedure for immunohistochemistry (IHC) confirmation of FRα positivity
8. Patient's tumor must be positive for FRα expression as defined by the Ventana FOLR1 Assay
9. Prior anticancer therapy:
9.1. Patients must have received at least 2 prior systemic lines of platinum therapy and be considered by the Investigator as appropriate for single-agent non-platinum therapy (documentation required eg, high risk of hypersensitivity reaction; risk of further cumulative toxicity with additional platinum, including but not limited to myelosuppression, neuropathy, renal insufficiency or other)Note: Patients who have had a documented platinum allergy may have had only 1 prior line of platinum
9.2. Patients may have received up to but no more than 1 prior independent non-platinum cytotoxic therapy
9.3. Patients must have had testing for BRCA mutation (tumor or germline) and, if positive, must have received a prior poly (ADP-ribose) polymerase (PARP) inhibitor as either treatment or maintenance therapy
9.4. Neoadjuvant ± adjuvant therapies are considered 1 line of therapy
9.5. Maintenance therapy (eg, bevacizumab, PARP inhibitors) will be considered part of the preceding line of therapy (ie, not counted independently)
9.6. Therapy changed due to toxicity in the absence of progression will be considered part of the same line (ie, not counted independently)
10. Patients must have completed prior therapy within the specified times below:
10.1. Systemic antineoplastic therapy within 5 half-lives or 4 weeks (whichever is shorter) prior to first dose of MIRV
10.2. Focal radiation completed at least 2 weeks prior to first dose of MIRV
11. Patients must have stabilized or recovered (Grade 1 or baseline) from all prior therapy-related toxicities (except alopecia)
12. Patients must have completed any major surgery at least 4 weeks prior to first dose of MIRV and have recovered or stabilized from the side effects of prior surgery prior to first dose of MIRV
13. Patients must have adequate hematologic, liver and kidney functions defined as:
13.1. Absolute neutrophil count (ANC) ≥ 1.5 x 10^9/L (1500/μL) without granulocyte colony-stimulating factor (G-CSF) in the prior 10 days or long-acting white blood cell (WBC) growth factors in the prior 20 days
13.2. Platelet count ≥ 100 x 10^9/L (100,000/μL) without platelet transfusion in the prior 10 days
13.3. Hemoglobin ≥ 9.0 g/dL without packed red blood cell (PRBC) transfusion in the prior 21 days
13.4. Serum creatinine ≤ 1.5 x upper limit of normal (ULN)
13.5. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 3.0 x ULN
13.6. Serum bilirubin ≤ 1.5 x ULN (patients with documented diagnosis of Gilbert syndrome are eligible if total bilirubin < 3.0 x ULN)
13.7. Serum albumin ≥ 2 g/dL

14. Patients must be willing and able to sign the informed consent form (ICF) and to adhere to the protocol requirements
15. Women of childbearing potential (WCBP) must agree to use highly effective contraceptive method(s) while on MIRV and for at least 3 months after the last dose
16. WCBP must have a negative pregnancy test within the 4 days prior to the first dose of MIRV

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Key exclusion criteria
1. Patients with endometrioid, clear cell, mucinous, or sarcomatous histology, mixed tumors containing any of the above histologies, or low-grade/borderline ovarian tumor
2. Patients with prior wide-field radiotherapy (RT) affecting at least 20% of the bone marrow
3. Patients with > Grade 1 peripheral neuropathy per Common Terminology Criteria for Adverse Events (CTCAE)
4. Patients with active or chronic corneal disorders, history of corneal transplantation, or active ocular conditions requiring ongoing treatment/monitoring, such as uncontrolled glaucoma, wet age-related macular degeneration requiring intravitreal injections, active diabetic retinopathy with macular edema, macular degeneration, presence of papilledema, and/or monocular vision
5. Patients with serious concurrent illness or clinically relevant active infection, including, but not limited to the following:a. Active hepatitis B or C infection (whether or not on active antiviral therapy)b. HIV infectionc. Active cytomegalovirus infectiond. Any other concurrent infectious disease requiring IV antibiotics within 2 weeks prior to the first dose of MIRV
Note: Testing at screening is not required for the above infections unless clinically indicated.
6. Patients with a history of multiple sclerosis (MS) or other demyelinating disease and/or Lambert-Eaton syndrome (paraneoplastic syndrome)
7. Patients with clinically significant cardiac disease including, but not limited to, any of the following:
7.1. Myocardial infarction ≤ 6 months prior to first dose
7.2. Unstable angina pectoris
7.3. Uncontrolled congestive heart failure (New York Heart Association > class II)
7.4. Uncontrolled ≥ Grade 3 hypertension (per CTCAE)
7.5. Uncontrolled cardiac arrhythmias
8. Patients with a history of hemorrhagic or ischemic stroke within 6 months prior to enrollment
9. Patients with a history of cirrhotic liver disease (Child-Pugh Class B or C)
10. Patients with a previous clinical diagnosis of noninfectious interstitial lung disease (ILD), including noninfectious pneumonitis
11. Patients requiring use of folate-containing supplements (eg, folate deficiency)
12. Patients with prior hypersensitivity to monoclonal antibodies (mAb)

13. Women who are pregnant or breastfeeding
14. Patients who received prior treatment with MIRV or other FRα-targeting agents
15. Patients with untreated or symptomatic central nervous system (CNS) metastases
16. Patients with a history of other malignancy within 3 years prior to enrollment
Note: patients with tumors with a negligible risk for metastasis or death (eg, adequately controlled basal-cell carcinoma or squamous-cell carcinoma of the skin, or carcinoma in situ of the cervix or breast) are eligible.
17. Prior known hypersensitivity reactions to study drugs and/or any of their excipients

Date of first enrolment
01/10/2022

Date of final enrolment
28/02/2023

Locations

Countries of recruitment
United Kingdom

Australia

Belgium

Canada

France

Germany

Ireland

Italy

Spain

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Immunogen Biopharma (Ireland) Limited

Funder(s)

Funder type
Industry

Funder Name
ImmunoGen

Alternative Name(s)
ImmunoGen, Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No