EGETIS THERAPEUTICS

POLAR-M

A study to learn about PledOx for nerve damage from chemotherapy in participants with previously untreated metastatic colorectal cancer

Thank you

Thank you to the participants who took part in this study. People who participate in clinical studies have a valuable role to play in medical research. The participants in this study had **previously untreated metastatic colorectal cancer** and helped the researchers to learn more about using PledOx for the prevention of nerve damage in the hands and feet from chemotherapy.

- PledOx is also known as calmangafodipir.
- Nerve damage from chemotherapy is also known as chemotherapy-induced peripheral neuropathy, or CIPN.

Overall, the results of this study suggest that **PledOx did not help prevent CIPN** in participants with previously untreated metastatic colorectal cancer.

The results shown in this summary are from 2 clinical studies. The results of many different studies are needed to know what treatments work best. Please talk to your doctor about your treatment options.

This study was sponsored by Egetis Therapeutics AB and Solasia Pharma K.K. This summary was prepared by a company independent of Egetis and Solasia. It has been reviewed by employees of Egetis.

How to say...

Peripheral neuropathy: *"per-IF-er-all nyoor-OP-uh-thee"*
Oxaliplatin: *"ox-A-lee-plat-in"*
5-fluorouracil: *"five flur-o-YOOR-uh-sill"*

What was this study about?

Chemotherapy is a common treatment for lots of different cancers. Oxaliplatin and 5-fluorouracil, also called 5-FU, are 2 common chemotherapy treatments that are usually taken together with folinic acid. Oxaliplatin can cause nerve damage in the hands and feet. This type of nerve damage is known as **chemotherapy-induced peripheral neuropathy**, also called CIPN.

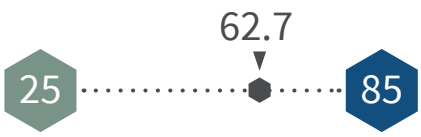
CIPN happens when the nerves that carry messages to the brain from the hands and feet and other parts of the body become damaged. This causes symptoms that can include tingling, numbness, and pain.

The study drug, PledOx, was being studied as a treatment to prevent CIPN. Researchers think that using PledOx while getting chemotherapy could help to prevent the nerve damage.

The aim of this study was to find out if getting PledOx in combination with chemotherapy helped to prevent CIPN symptoms in participants with previously untreated metastatic colorectal cancer. 'Metastatic' means that the cancer has spread into other organs and parts of the body not close to the organ that it started in.

Who was in this study?

This study included **291** participants in Belgium, the Czech Republic, France, Germany, Hong Kong, Hungary, Italy, Japan, South Korea, Spain, Taiwan, the United Kingdom, and the United States.



The participants were **25** to **85** years old when they joined the study. The average age was **62.7** years old.

41.8% were female and **58.2%** were male.

50.9% were White
42.1% were Asian
0.7% were Black or African American
6.3% were of unknown race

All of the participants had previously untreated metastatic colorectal cancer and were supposed to start getting chemotherapy treatment with oxaliplatin, 5-FU, and folinic acid from their own doctors.

What happened in this study?

This study started in November 2018 and was planned to last for about 3 years. However, the researchers decided to stop the study early because of safety concerns related to allergic reactions, following guidance from the regulatory authorities. So the study was ended in August 2020.

The participants got either **PledOx or a placebo**, along with their oxaliplatin, 5-FU, and folinic acid chemotherapy. A placebo looks like a drug but does not have any medicine in it. Researchers use placebos to make sure that any effects are actually caused by the study drug. There were 2 different doses of PledOx that the participants could get. The doses were measured in "micromoles per kilogram of body weight", also known as "µmol/kg".

In total:

- 97 participants were supposed to get 2 µmol/kg of PledOx
- 96 participants were supposed to get 5 µmol/kg of PledOx
- 98 participants were supposed to get the placebo

This was a **double-blind** study. This means that none of the participants, researchers, study doctors or other study staff knew what study treatment each participant was getting. This was also a **randomized** study. This means that the researchers used a computer program to randomly allocate one of the study treatments to each participant. Researchers do this so that the groups have similar participants and the results of each study treatment can be compared as accurately as possible.

All of the study treatments were given through a needle into a vein, also known as an intravenous infusion, or an **IV infusion**. Before each dose of study treatment, all of the participants also got an IV infusion of 2 common drugs called diphenhydramine and ranitidine. This was to help in case any of the participants had an allergic reaction.

The participants were to visit their study sites every 2 weeks for 24 weeks to get their dose of study treatment. This was to be 12 doses in total. After the 12 doses, some participants could continue getting more doses. Because the study ended early, most of the participants ended up having fewer than 12 doses.

At these visits, the study doctors:

- Asked the participants to complete questionnaires and did several tests and measurements to find out about their CIPN symptoms
- Did a physical examination and checked the health of the participants
- Asked about any medications or medical problems that the participants could be having
- Took blood samples

At some of these visits, the study doctors also:

- Checked the health of the participants' hearts using an ECG, also known as an electrocardiogram
- Took scans of the participants' cancers using MRI or CT scans, also known as magnetic resonance imaging and computed tomography, to measure their cancer

After the participants finished getting all of their doses of study treatment, they were planned to continue visiting their study site for up to 9 more visits. This was so that the study doctors could continue to monitor the health of the participants for any long-term effects.

Because of the COVID-19 pandemic, many of these study site visits were done by a telephone call instead.

What were the results of this study?

The main questions that the researchers wanted to answer in this study were:

- Did PledOx prevent the participants' moderate-to-severe CIPN symptoms when measured with a certain questionnaire?
- Did PledOx prevent the participants' CIPN symptoms when measured with other tests and measurements?

The results below are for 236 out of 291 participants who had results available from at least 1 of the tests and measurements. Because the study was stopped early, the researchers did not have as many participants as they originally planned to have. This meant they also did not have enough data to be absolutely certain about the results.

Did PledOx prevent the participants' moderate-to-severe CIPN symptoms when measured with a certain questionnaire?

To answer this question, the researchers asked the participants to answer a questionnaire at different times throughout the study. This questionnaire was called the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity-13-item subscale, also known as **FACT/GOG-NTX**. The questionnaire lists 13 different symptoms and asks the participants to give each symptom a score from 0 to 4, with a higher score meaning more severe symptoms. In this study, the researchers only looked at the participants' answers to 4 of the questions.

The researchers looked at how many participants had moderate-to-severe CIPN symptoms after 9 months of getting their study treatment. They compared the results for the participants who got the placebo with the participants who got 2 µmol/kg of PledOx and with the participants who got 5 µmol/kg of PledOx.

Overall, the researchers found that there were **no important differences between the 3 study treatment groups in this study**.

The researchers also wanted to look at these results in combination with another very similar study that was happening at the same time, called the POLAR-A study. The POLAR-A study also looked at PledOx for the prevention of CIPN and measured the participants' moderate-to-severe CIPN using the 4 questions from the FACT/GOG-NTX questionnaire.

When the researchers looked at the results of these 2 studies together, they found that the combined results for both studies match the results from the POLAR-A study alone. This was that there was a difference between the participants who got the placebo and the participants who got 5 µmol/kg of PledOx. Overall, the participants who got the placebo had fewer moderate-to-severe CIPN symptoms than the participants who got 5 µmol/kg of PledOx.

The results of this study suggest that PledOx did not help prevent CIPN in participants with previously untreated metastatic colorectal cancer.

Did PledOx prevent the participants' CIPN symptoms when measured with other tests and measurements?

To answer this question, the researchers did several tests and measurements and asked the participants to complete questionnaires at different times throughout the study. These included finding out about:

- Sensitivity to touching cold items, using a questionnaire
- Amount of chemotherapy given and any changes to the doses, if they were needed
- Sensitivity to vibrations, using a vibrating tuning fork held against the participants' ankles
- Pain in the participants' hands and feet, using a questionnaire
- Fine motor skills or hand dexterity, using a tool called a grooved pegboard

The researchers compared the results for each of these tests and measurements for the participants who got the placebo with the participants who got 2 µmol/kg of PledOx and with the participants who got 5 µmol/kg of PledOx.

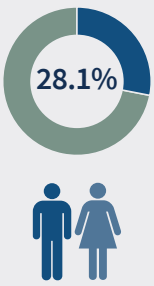
Overall, the researchers found that there were no important differences in any of these tests and measurements between the 3 treatment groups in this study.

What were the safety results of this study?

During clinical studies, participants are asked to report if they feel unwell or notice anything different about their bodies. All of these signs and symptoms that participants have during a study are called **adverse events**. Adverse events that are life-threatening, cause lasting problems, or require hospital care are known as **serious adverse events**.

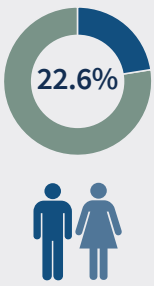
The results below are for 285 out of 291 participants who got at least 1 dose of their study treatment.

Serious adverse events



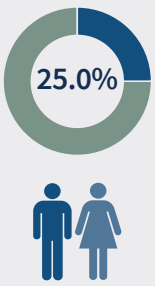
There were **28.1%** of the participants who got 2 µmol/kg of PledOx who had any serious adverse event.

This was **27** out of **96** participants.



There were **22.6%** of the participants who got 5 µmol/kg of PledOx who had any serious adverse event.

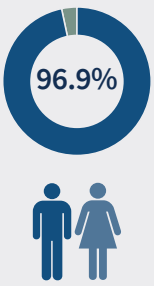
This was **21** out of **93** participants.



There were **25.0%** of the participants who got the placebo who had any serious adverse event.

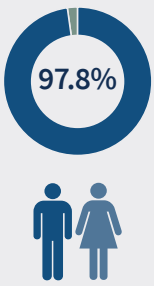
This was **24** out of **96** participants.

Adverse events



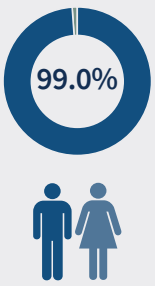
There were **96.9%** of the participants who got 2 µmol/kg of PledOx who had any adverse event.

This was **93** out of **96** participants.



There were **97.8%** of the participants who got 5 µmol/kg of PledOx who had any adverse event.

This was **91** out of **93** participants.



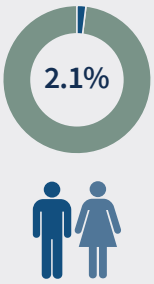
There were **99.0%** of the participants who got the placebo who had any adverse event.

This was **95** out of **96** participants.

If the study doctors think an adverse event may be related to the study drug, it is called an **adverse reaction**. Adverse reactions that are life-threatening, cause lasting problems, or require hospital care are known as **serious adverse reactions**.

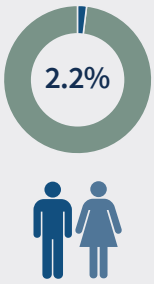
The adverse reactions presented below may or may not be definitely caused by the study drug. It takes many studies to know if a drug definitely causes an adverse reaction.

Serious adverse reactions



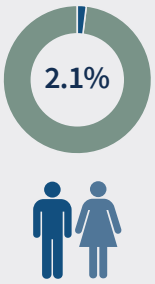
There were **2.1%** of the participants who got 2 µmol/kg of PledOx who had serious adverse reactions.

This was **2** out of **96** participants.



There were **2.2%** of the participants who got 5 µmol/kg of PledOx who had serious adverse reactions.

This was **2** out of **93** participants.



There were **2.1%** of the participants who got the placebo who had serious adverse reactions.

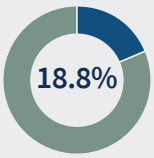
This was **2** out of **96** participants.

The table below shows the serious adverse reactions that happened during the study and how many participants had these serious adverse reactions. Some participants may have had more than 1 serious adverse reaction.

Serious adverse reactions	**2 µmol/kg of PledOx** (out of 96 participants)	**5 µmol/kg of PledOx** (out of 93 participants)	**Placebo** (out of 96 participants)
A change in mental state or consciousness	1.0% (1)	0.0% (0)	0.0% (0)
A reaction at the infusion site	1.0% (1)	0.0% (0)	0.0% (0)
Feeling faint	1.0% (1)	0.0% (0)	0.0% (0)
Nausea	1.0% (1)	0.0% (0)	0.0% (0)
Vomiting	1.0% (1)	0.0% (0)	0.0% (0)
A blood clot in a vein leading from the ovaries	0.0% (0)	1.1% (1)	0.0% (0)
A fever with low levels of a type of white blood cell called a neutrophil	0.0% (0)	1.1% (1)	0.0% (0)
Low levels of potassium in the blood	0.0% (0)	1.1% (1)	0.0% (0)
High levels of potassium in the blood	0.0% (0)	0.0% (0)	1.0% (1)
Kidney failure	0.0% (0)	0.0% (0)	1.0% (1)

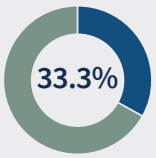
None of the participants died because of serious adverse reactions during this study.

Adverse reactions



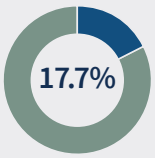
There were **18.8%** of the participants who got 2 µmol/kg of PledOx who had adverse reactions.

This was **18** out of **96** participants.



There were **33.3%** of the participants who got 5 µmol/kg of PledOx who had adverse reactions.

This was **31** out of **93** participants.



There were **17.7%** of the participants who got the placebo who had adverse reactions.

This was **17** out of **96** participants.

The table below shows the adverse reactions that happened in at least 5.0% or more of participants in any study drug group during the study. It also shows how many participants had these adverse reactions. Some participants may have had more than 1 adverse reaction.

Adverse reactions	**2 µmol/kg of PledOx** (out of 96 participants)	**5 µmol/kg of PledOx** (out of 93 participants)	**Placebo** (out of 96 participants)
Diarrhea	7.3% (7)	4.3% (4)	4.2% (4)
Low levels of a type of white blood cell called a neutrophil	5.2% (5)	5.4% (5)	3.1% (3)
Fatigue	5.2% (5)	4.3% (4)	5.2% (5)
Nerve damage in the hands and feet, also known as peripheral neuropathy	5.2% (5)	3.2% (3)	1.0% (1)
Nausea	2.1% (2)	5.4% (5)	4.2% (4)
Rash	0.0% (0)	6.5% (6)	2.1% (2)

What did the researchers learn from this study?

Overall, the results of this study suggest that PledOx did not help prevent CIPN in participants with previously untreated metastatic colorectal cancer.

The results shown in this summary are from only 2 clinical studies. Other studies may provide new information or different results. Please talk to your doctor about your treatment options.

Further clinical studies of PledOx for CIPN are not planned.

More information

You can find more information about this study on the website listed below. When a full report of the study results is available, it can also be found using these details.

Go to www.clinicaltrials.gov and search for **NCT03654729**

For more information about CIPN and current treatments available, please speak to a healthcare professional. If you have questions about this study, please contact the sponsor, Egetis, at **info@egetis.com**

Full study title: A Phase 3, Double-blind, Multicenter, Placebo-controlled Study of PledOx Used on Top of Modified FOLFOX6 (5 FU/FA and Oxaliplatin) to Prevent Chemotherapy Induced Peripheral Neuropathy (CIPN) in Patients With First-line Metastatic Colorectal Cancer

Egetis protocol number: PP06490

National Clinical Trials number: NCT03654729

Egetis thanks all of the participants who took part in this study. Their support is necessary to help researchers answer important health questions and find new medical treatments.

Glossary

Term	Meaning
5-fluorouracil, or 5-FU	A type of chemotherapy
Adverse reaction	Any sign or symptom that a participant has during a study that the study doctors think could be possibly related to the study drug
Chemotherapy-induced peripheral neuropathy, or CIPN	Nerve damage in the hands and feet caused by chemotherapy
Colorectal cancer	Cancer that starts in the colon or rectum, also known as bowel cancer
Diphenhydramine	A common medicine for allergic reactions, called an antihistamine
Double-blind	When none of the participants, researchers, study doctors, or other study staff know what study treatment each participant is getting
Electrocardiogram, or ECG	A way to measure heart health by placing wire sensor pads around the body
Fine motor skills or hand dexterity	The ability to do coordinated tasks with hand and finger muscles
Folinic acid	A vitamin given with chemotherapy
Intravenous infusion, or IV infusion	A way to deliver a drug through a needle into a vein
Magnetic resonance imaging and computed tomography, or MRI and CT	Methods for scanning the inside of the body
Metastatic cancer	Cancer that has spread to other organs and parts of the body not close to the organ it started in
Oxaliplatin	A type of chemotherapy
PledOx, or calmangafodipir	The study drug in this study
Placebo	A dummy drug that has no medicine in it, such as a sugar pill or salt water
Randomized	When a computer program is used to randomly choose what study treatment each participant gets
Ranitidine	A common medicine for allergic reactions, called an antihistamine
Serious adverse reaction	An adverse reaction that is life-threatening, causes lasting problems, or requires hospital care

The final clinical study report that this summary is based on is dated August 25, 2021.

This summary was last updated on August 31, 2021.