CLINICAL STUDY RESULTS

A Study to Assess the Effects and Safety of Irinotecan Liposome Injection in People Who Had Not Received Chemotherapy for Cancer of the Pancreas That Has Spread to Other Parts of the Body

Participants who received irinotecan liposome injection lived 2 months longer compared with participants who received standard first-line treatment.
No new safety concern with the study drug was found.

The results shown in this summary are from one clinical study. Other clinical studies may produce different results.

The objective of this document is to convey the results of the study in simple language to a lay reader.

This lay summary was created by Ipsen with the assistance of a third party writing service provider.

What was the study about?

This study, called NAPOLI 3, is a clinical study to learn about a treatment called irinotecan liposome injection for people with metastatic pancreatic ductal adenocarcinoma.

Metastatic pancreatic ductal adenocarcinoma is a type of cancer that starts in the pancreas and then spreads to other parts of the body. Pancreatic cancers are hard to diagnose early as they often have no early warning signs. Treatments aim to shrink the cancer and slow its spread to keep patients alive with a good quality of life for as long as possible.

Irinotecan is a medicine that works by blocking a protein called Topoisomerase-1 that helps cells multiply. When Toposiomerase-1 becomes too active, it can cause cancer cells to grow. By blocking Topoisomerase-1, irinotecan helps stop the cancer from growing.

Liposomal irinotecan injection is a form of irinotecan that is wrapped in a fat bubble called a liposome. The fat bubble stops irinotecan from being broken down by the body right away. This means that it can stay in the bloodstream for longer and work more effectively.

In this study, researchers compared the effects and safety of a combination treatment called NALIRIFOX containing irinotecan liposome injection to a standard first-line combination treatment—nab-paclitaxel given with gemcitabine (Gem+NabP). The details of each treatment are mentioned further in this document.

> The aim of this study was to compare the effects and safety of NALIRIFOX with Gem+NabP in participants who had not received chemotherapy for cancer of the pancreas that has spread to other parts of the body.

The study started in February 2020. It was conducted at 187 hospital centers in 18 countries worldwide. Although the results of the main question were assessed till July 2022 as planned, the study continued to collect more information on the safety of the study drugs. The study ended in February 2025.

Who took part in this study?

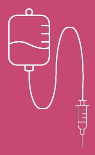
To be eligible to take part in the study, participants had to be:

- aged 18 years or older
- diagnosed with cancer of pancreas that had spread to other part(s) of the body, and
- able to perform normal daily tasks and take care of themselves.

Participants were not eligible to take part in the study if:

- they had been treated for cancer of the pancreas with medicines, chemotherapy, radiation or surgery,
- they had a health condition that made them illegible to participate, as advised by a doctor.

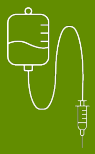
What treatments were used?



NALIRIFOX (Study treatment)

The following drugs were given into the vein on Days 1 and 15 of each cycle. Participants received these treatments in cycles. Each cycle was 28 days long.

- **irinotecan liposome injection** 50 mg/m^2**,**
- **oxaliplatin** 60 mg/m^2 infusion**,**
- **5-fluorouracil** 2400 mg/m^2**, and**
- **leucovorin** 400 mg/m^2 infusion.



Gem + NabP (Standard treatment)

The following drugs were given into the vein on Days 1, 8 and 15 of each cycle. Participants received these treatments in cycles. Each cycle was 28 days long.

- **Nab-paclitaxel** 125 mg/m^2 infusion, and
- **Gemcitabine** 1000 mg/m^2 infusion.

Note: mg/m^2 is a way to measure the drug dose given to participants. For example, 50 mg/m^2 means 50 milligrams will be given for each square meter (area) of a participant's body.

The study was conducted in three stages

Screening: The study doctor checked if participants could take part in this study, based on defined criteria. This was done within 28 days before starting the treatment.

Treatment: 770 eligible participants were assigned randomly to one of the two treatment arms based on: their ability to perform normal daily tasks and take care of themselves, where they lived, and whether the cancer had spread to their liver.

Out of the 770 participants randomly assigned, 749 received the study treatment presented as follows:

- **NALIRIFOX Arm** (370 participants)
- **Gem + NabP Arm** (379 participants)

21 participants have not received the study treatment because they decided to leave the study, their cancer worsened before the start of the treatment, or they ended up not being eligible to take part in the study.

If a participant's cancer got worse or they had an unacceptable adverse effect due to the study treatment, the treatment was stopped.

This was an "open-label" study. This means that the participants and the study team knew which treatments the participants would receive. The participants' health was monitored throughout the study by the study doctor.

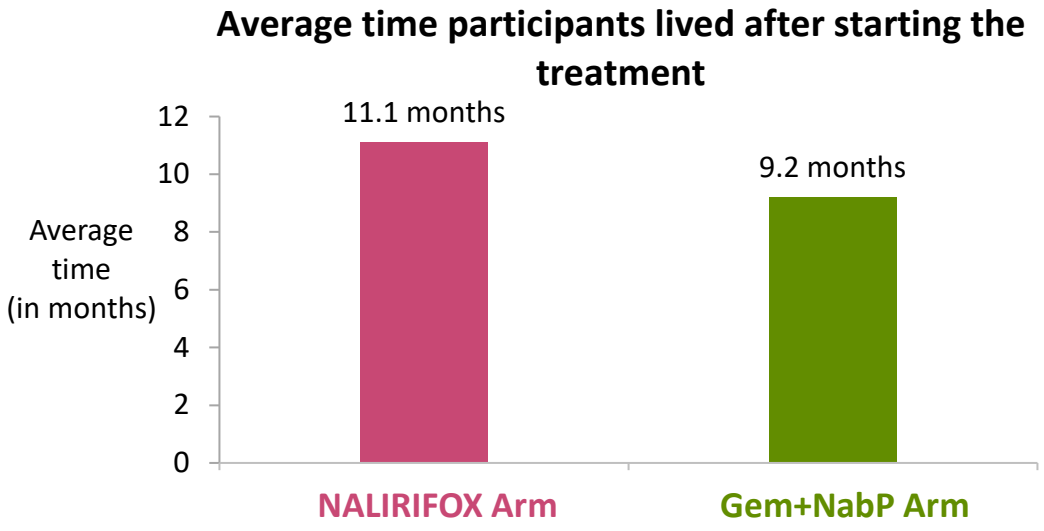
Follow-up: Participants returned to the study site one month after their last dose of study treatment for health evaluation performed by the doctor. After that, they were followed up every two months by telephone, email, or a clinic visit until the study ended, to confirm their overall health and wellbeing.

What researchers found out in the study?

Participants treated with NALIRIFOX lived for 2 months longer than those who received nab-paclitaxel and gemcitabine

How long did the participants on NALIRIFOX live after the start of the treatment compared with those on Gem+NabP?

On average, participants on NALIRIFOX lived 2 months longer (11.1 months) compared with participants on Gem+NabP (9.2 months) after the start of the treatment.



How long did participants on NALIRIFOX live without their cancer getting worse compared to those on Gem+NabP?

Participants on NALIRIFOX lived 7.4 months without their cancer getting worse, compared to 5.6 months for those who were on Gem+NabP.

How many participants on NALIRIFOX had their cancer decrease or completely disappear compared to those on Gem+NabP?

42% (160 out of 383) of participants on NALIRIFOX had their cancer decrease or completely disappear, compared to 36% (140 out of 387) of participants on Gem+NabP.

How did the treatment make participants feel?

During the study, participants were asked to report any 'adverse events', i.e. if they felt unwell, experienced any kind of medical event, or noticed anything different about their bodies. Researchers recorded all adverse events reported by participants, whatever the cause.

If the study doctor thinks an adverse event may be related to the study treatment, it is called a 'side effect'. In this document we have only presented the side effects. A side effect is considered 'serious' when it is life-threatening, causes lasting problems, or leads to hospitalization.

- Adverse events that are life-threatening, cause lasting problems or require an individual to go to the hospital are considered serious.
- 23% participants (171 out of 749) experienced serious side effects.
- 2% participants (14 out of 749) died due to side effects. Most died during follow-up stage.

94% (704 out of 749) participants experienced side effects. 25% (190 out of 749) participants stopped study treatment due to a side effect. The overall summary of side effects in each group is presented below:

Participants who	NALIRIFOX (370 Participants)	Gem + NabP (379 Participants)
Had any side effects	95% (352 out of 370) 	93% (352 out of 379) 
Had serious side effects	27% (99 out of 370) 	19% (72 out of 379) 
Stopped treatment due to a side effect	27% (100 out of 370) 	24% (90 out of 379) 
Died due to a side effect	2% (6 out of 370)	2% (8 out of 379)

The most common serious side effects participants experienced in any group were diarrhoea, vomiting, and feeling sick (the desire to vomit).

The most common side effects that happened in more than 25% of the participants in any group are shown in the table below. They are shown as percentage (%) followed by the actual number of participants in the arm (for example, 64% or 238 out of 370).

There were no new safety concerns for either of the combinations.

Side Effects (more than 25% of participants)	NALIRIFOX (370 Participants)	Gem + NabP (379 Participants)
Diarrhoea	64% (238 out of 370) 	27% (101 out of 379) 
Feeling sick (the desire to vomit)	54% (199 out of 370) 	35% (134 out of 379) 
Vomiting	33% (123 out of 370) 	20% (77 out of 379) 
Decrease in appetite	29% (106 out of 370) 	18% (68 out of 379) 
Extreme tiredness	29% (106 out of 370) 	30% (114 out of 379) 
Low neutrophil count (white blood cells that protect from infection)	28% (103 out of 370) 	31% (116 out of 379) 
Low number of red blood cells	21% (76 out of 370) 	34% (127 out of 379) 
Hair loss	14% (50 out of 370) 	31% (117 out of 379) 

More information

To learn more about this study, please visit the ClinicalTrials.gov website and search for study NCT04083235. Or visit the Clinicaltrialsregister.eu/ctr-search/search website and search for study 2018-003585-14.

For more information about current treatments available, please speak to your healthcare provider. If you have any questions about this study, please contact the sponsor, Ipsen at:

clinical.trials@ipsen.com

Future research

No future studies are planned on this topic.

Study identification and other information

FULL STUDY TITLE: An Open-Label, Randomised, Multicentre, Phase III Study of Irinotecan Liposome Injection, Oxaliplatin, 5-Fluorouracil/Leucovorin Versus Nab-Paclitaxel Plus Gemcitabine in Subjects Who Have Not Previously Received Chemotherapy for Metastatic Adenocarcinoma of The Pancreas (NAPOLI 3).

STUDY NUMBERS: Europe: 2018-003585-14 | United States: NCT04083235 |

PROTOCOL: D-US-60010-001.

OTHER INFORMATION: Phase III studies can take several months to years to complete and look at how safe a potential new treatment is.

We thank all the volunteers who took part in this study and their caregivers who supported them. Without their support, advances in treatments for medical conditions would not be possible.

We would also like to thank the people who took the time to review this document to make it easier for a general audience to read.