CLINICAL STUDY RESULTS

A study comparing the effects of liposomal irinotecan with the standard treatment in people whose lung cancer worsened after initial treatment

Irinotecan liposomal injection has a similar effect to the standard treatment, topotecan, in people with lung cancer that worsened after initial treatment.

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

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

What was the study about?

This study was done in 2 parts. The aim of Part 1 was to find a safe dose of irinotecan liposomal injection. The aim of Part 2 was to compare the effects of irinotecan liposome injection with topotecan. The results of Part 2 are explained in this summary. This study was performed in people who had small cell lung cancer (SCLC) that worsened after initial treatment.

SCLC is a type of fast-growing cancer that forms in the tissues of the lung. The cells of this type of cancer are very small and look like oats under the microscope. It spreads very fast to other parts of the body such as the brain, liver, adrenal glands, bone, and bone marrow. SCLC often gets detected late due to a lack of specific symptoms. Although treatments are available for people with SCLC, these treatments aren't always effective over the long term.

Irinotecan is a drug that blocks a protein called topoisomerase-1, which helps cancer cells to grow.

Irinotecan liposomal injection is a type of treatment where irinotecan is wrapped in a fat bubble called a liposome. The fat bubble stops irinotecan from being broken down straight away by the body. This means that irinotecan can stay in the bloodstream for longer and work more effectively by specifically targeting the tumor.

In this study, researchers wanted to compare the effects and safety of irinotecan liposomal injection with another drug called topotecan, which works in a similar way to irinotecan.

The aim of this study was to compare the effects of irinotecan liposomal injection with topotecan in participants with SCLC that worsened after initial treatment

The study took place between April 2018 and February 2022 at 110 study sites around the world.

Who took part in this study?

461
PARTICIPANTS

313
MEN

148
WOMEN

62 YEARS
AVERAGE AGE

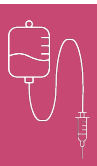
To be eligible to take part in the study, participants had to:

- be aged 18 years or older
- be able to perform normal daily tasks and take care of themselves
- have life expectancy of at least 3 months
- be diagnosed with SCLC that worsened after initial treatment

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

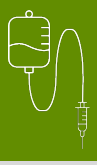
- they had been treated with certain medicines or had certain health conditions that could interfere with the study results

What treatments were used?



Irinotecan liposome injection was given at a dose of 70 mg/m^2 into the vein for one and a half hours every 2 weeks in each cycle.

Participants received these treatments in cycles. Each cycle was 6 weeks long.



Topotecan was given at a dose of 1.5 mg/m^2 into the vein for half an hour daily for 5 days and then every 3 weeks in each cycle.

Participants received these treatments in cycles. Each cycle was 6 weeks long.

Note: mg/m^2 is a way to measure the drug dose given to participants. For example, 70 mg/m^2 means 70 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. This was done within 28 days before starting treatment.

Treatment: 461 participants were eligible for the study. They were assigned randomly to one of the two treatment groups using a computer - this process is called randomization. Randomization means that each participant could be assigned to any group, which helps to make sure the groups are distributed fairly.

Overall, 449 participants received treatment.

- **Group 1: Irinotecan liposome injection group** (226 participants)
- **Group 2: Topotecan group** (223 participants)

12 participants were randomized but could not receive the study treatment for different reasons.

A participant's treatment was stopped if their cancer worsened or they had an unacceptable adverse event due to the study treatment.

This was an “open-label” study. This means that the participants and the study team both knew which treatments the participants would receive. Participants’ health was monitored throughout the study by the study doctor.

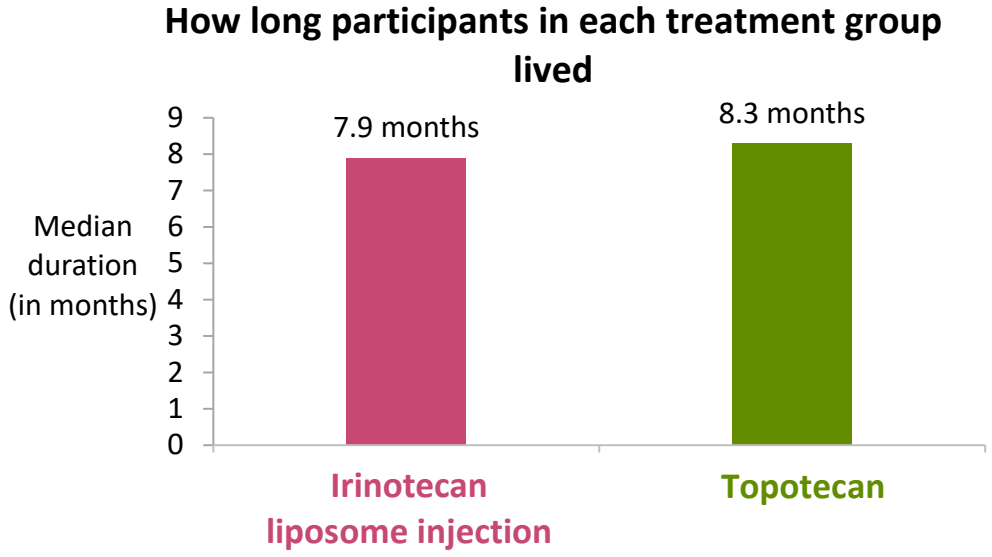
Follow-up: Participants returned to the study site one month after their last dose of study treatment for a health check. After that, participants were followed up every month by telephone, email, or a clinic visit until the study ended to confirm their overall health and wellbeing.

What did researchers find out in this study?

Participants randomized to receive Irinotecan liposome injection and those randomized to receive topotecan lived for a similar duration of time after starting treatment.

After randomization, how long did the participants randomized to receive irinotecan liposome injection live, compared to those randomized to receive topotecan?

After randomization, participants randomized to receive irinotecan liposome injection lived for a median duration of 7.9 months, compared with participants randomized to receive topotecan, who lived for a median duration of 8.3 months.



The "median" is the middle value of survival time in a group of numbers.

For example, when we say the median duration was 7.9 months, it means that half of the participants lived longer than 7.9 months, and half lived less than 7.9 months.

How long did participants live without their cancer getting worse?

Participants randomized to receive irinotecan liposome injection lived a median duration of 4.0 months without their cancer getting worse, while those randomized to receive topotecan lived for a median duration of 3.2 months without their cancer getting worse.

How many participants had an overall reduction in their cancer?

44.1% of participants randomized to receive irinotecan liposome injection had an overall reduction in their cancer, compared to 21.6% of those randomized to receive topotecan.

What did participants say about how they felt while they were receiving treatment?

There wasn't enough data available to answer this question.

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'. 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.
- 24% of participants (106 out of 449) experienced serious side effects.
- 1% of participants (5 out of 449) died due to side effects.

In total, 91% (409 out of 449) of participants experienced side effects:

- **Group 1: 86% (195 out of 226) of participants** who received **Irinotecan liposome injection** experienced side effects.
- **Group 2: 96% (214 out of 223) of participants** who received **Topotecan** experienced side effects.

4% (20 out of 449) of participants stopped study treatment due to a side effect.

The most commonly reported side effects that happened in more than 40% of the participants in either group are shown in the table below, both as a percentage (%) followed by the actual number of participants in the group (for example, 55% or 124 out of 226).

Side Effects	Irinotecan liposome injection (226 Participants)	Topotecan (223 Participants)
Diarrhea	55% (124 out of 226) 	14% (31 out of 223) 
Low number of red blood cells (anemia)	28% (64 out of 226) 	76% (170 out of 223) 
Low number of white blood cells called neutrophils	17% (38 out of 226) 	62% (139 out of 223) 
Low number of white blood cells called leukocytes	13% (29 out of 226) 	43% (95 out of 223) 
Low number of a type of blood cells called platelets	5% (11 out of 226) 	57% (128 out of 223) 

More information

To learn more about this study, please visit the ClinicalTrials.gov website and search for study NCT03088813 or visit clinicaltrialsregister.eu/ctr-search/search and search for 2017-004261-26.

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

There is no future research planned on this topic.

Study identification and other information

FULL STUDY TITLE: Resilient: A Randomized, Open Label Phase 3 Study of Irinotecan Liposome Injection (Onivyde®) Versus Topotecan in Patients With Small Cell Lung Cancer Who Have Progressed on or After Platinum-Based First-Line Therapy.

STUDY NUMBERS: Europe: 2017-004261-26| United States: NCT03088813 |

PROTOCOL: MM-398-01-03-04.

OTHER INFORMATION: Phase 3 studies can take several months to years to complete and look at how effective and safe a potential new treatment is.

We thank all the volunteers and their families/care givers who took part in this study. 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.