PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Study Number: IMMU-132-09

Dates of Study: May 2019 to October 2023

Short Study Title: Study of Sacituzumab Govitecan in Adults With Hormonal Receptor-Positive (HR+) Human Epidermal Growth Factor Receptor 2 (HER2) Negative Metastatic Breast Cancer (MBC) Who Have Failed at Least Two Prior Treatments

Study Nickname: TROPiCS-02

Date of this Plain Language Summary: August 2024
The information in this summary does not include any information available after this date.

Thank you

Thank you to the participants who contributed to the clinical study for **sacituzumab govitecan**, also known as **Trodelvy** or **IMMU-132**.

Gilead Sciences sponsored this study. We believe it is important to share the results with study participants and the general public.

If you participated in the study and have questions about the results, please speak with a doctor or staff member at the study site.

Always talk to a doctor or healthcare provider before making any treatment changes.

This document is a short summary of this study written for a general audience. Links to scientific summaries of this study can be found at the end of this document.

What was the purpose of the study?

The purpose of this study was to learn about the safety and how well treatment with **sacituzumab govitecan (SG)** works. Researchers compared SG with 4 common **chemotherapy** treatments of physician's (study doctor's) choice. Study participants had hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2−) metastatic breast cancer and received at least 2 prior treatments that did not work well or stopped working.

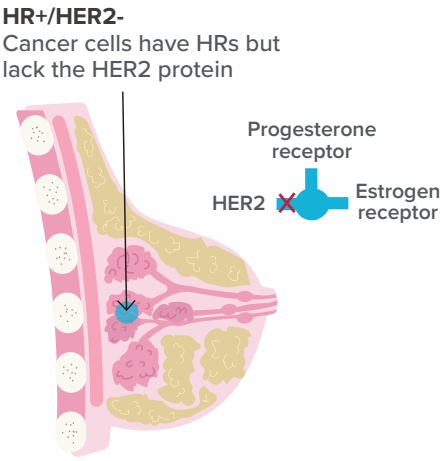
> **Chemotherapy** is a treatment for cancer that works by stopping the growth of cancer cells, either by killing the cells or stopping them from dividing.

What is HR+/HER2- metastatic breast cancer?

Breast cancer is a type of cancer where breast cells grow out of control and form a tumor. Cancer may spread to other parts of the body. When this happens, the cancer is called metastatic cancer.

There are certain proteins commonly found on the surface of breast cancer cells. Some of them are as follows:

- **Hormone receptors (HRs)** are the proteins that bind to hormones like estrogen and progesterone. This helps in the growth of cancer cells. HR-positive (HR+) means the breast cancer cells that have one or both hormone receptors present on them.
- **Human epidermal growth factor receptor (HER2)** is a protein that increases the rate at which the cancer cells grow. HER2-negative (HER2-) means that breast cancer cells have either no HER2 or low levels of HER2.



> A **receptor** is a part of a cell that binds to a specific substance. The binding triggers a particular change in the cell's activity.

Breast cancer is generally first treated with medicines that target these receptors. The presence of one or more of these receptors affects the growth of breast cancer cells and decides the treatments that can be used. Common treatments include hormonal therapy and chemotherapy. However, they may not work or may stop working in some people. Some cancer medicines may kill healthy cells along with the cancer cells. This may lead to side effects.

Antibody-drug conjugates (ADC) are a type of medicine that are designed to target only the cancer cells. SG is an ADC that works by attaching itself to a receptor found on the cancer cells. This helps to deliver the drug directly to cancer cells and stop them from growing and spreading.

SG has been approved for the treatment of another type of breast cancer, meaning it can be prescribed by doctors. It is now being studied to see if it could also be a possible treatment option for HR+/HER2- metastatic breast cancer.

This is a **Phase 3 clinical study**. This means that researchers looked at how SG worked in a large group of participants.

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

- How long did participants who got SG live without their cancer getting worse (known as **progression-free survival** or **PFS**) compared to participants who got chemotherapy?
- What side effects did participants have during the study, if any?

The other question the researchers wanted to answer in this study was:

- How long did participants who got SG live (known as **overall survival** or **OS**) compared to participants who got chemotherapy?

Who took part in the study?

543 people living with HR+/HER2- metastatic breast cancer in 9 countries around the world took part in this study.

People could take part in the study if they:

- Were at least 18 years of age
- Had HR+/HER2- metastatic breast cancer
- Had received at least 2 chemotherapies for metastatic breast cancer that did not work well or had stopped working

Participants were **27 to 86 years old** when they joined the study.

The table below shows how many study participants were from each country.

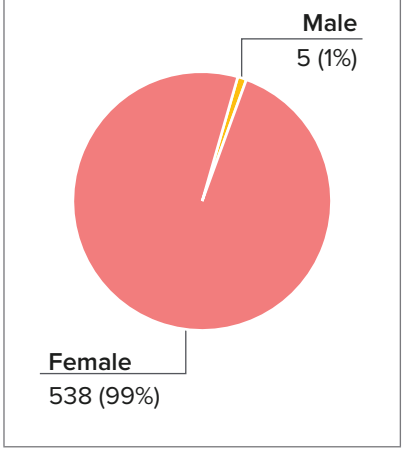
Country	Number of participants (%)
United States	228 (42%)
France	137 (25%)
Spain	69 (13%)
Germany	46 (8%)
Belgium	25 (5%)
Italy	15 (3%)
United Kingdom	14 (3%)
Netherlands	8 (1%)
Canada	1 (under 1%)

The sex, race, and ethnicity of participants are shown below.

Race	Number of participants (%)
White	362 (67%)
Unknown or not reported	139 (26%)
Black or African American	21 (4%)
Asian	16 (under 3%)
Other or more than one race	4 (under 1%)
Native Hawaiian or Other Pacific Islander	1 (under 1%)

Ethnicity	Number of participants (%)
Not Hispanic or Latino	426 (79%)
Unknown or not reported	99 (18%)
Hispanic or Latino	18 (3%)

Sex



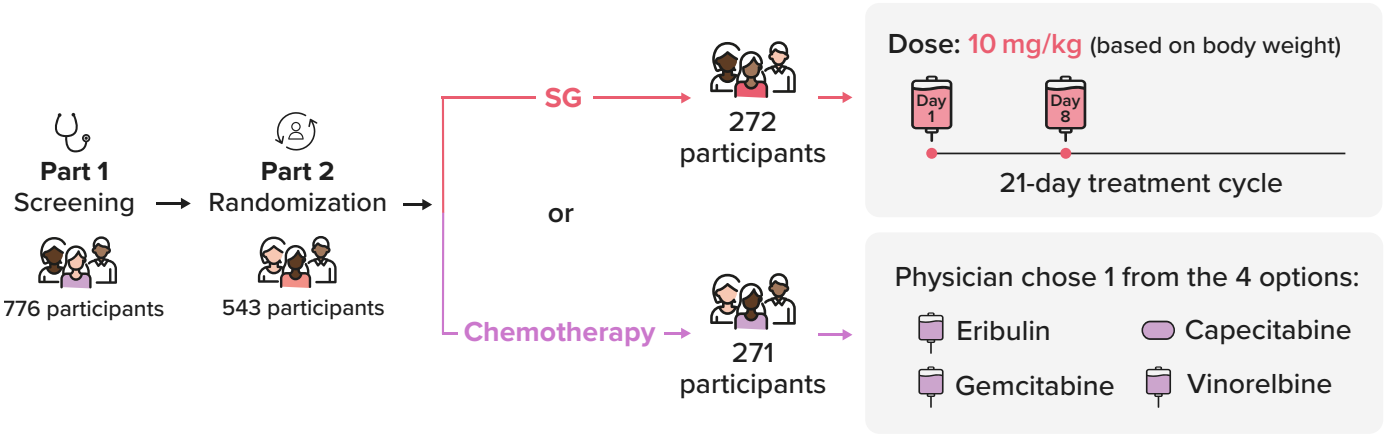
What happened during the study?

This was a **randomized** study, which means the researchers used a computer program to put participants into treatment groups by chance. This helped make sure the treatments were chosen fairly. This was also an open-label study, which means each participant knew what treatment they were taking, and the doctors and study staff also knew.

The study was conducted in 2 parts. Part 1 was the screening phase. During this part, study doctors checked to make sure each participant was a good fit for the study. They checked the participants' health and medical histories. Each participant had imaging scans before starting the study to see how far their cancer had spread. This part lasted for no more than 28 days. Part 2 was the randomization phase. Eligible participants screened from Part 1 entered Part 2 of the study.

Participants were randomized to receive either SG or chemotherapy as follows:

- **SG:** The dose was based on the participant's body weight. SG was given 10 mg/kg as an intravenous infusion, which is a slow injection into a vein, on Days 1 and 8 of every 21-day treatment cycle.
- **Chemotherapy:** The physician chose 1 out of 4 chemotherapy options commonly used for breast cancer. These included:
  - **Eribulin**: given as a slow injection into a vein in a 21-day treatment cycle.
  - **Capecitabine**: given by mouth in a 21-day treatment cycle.
  - **Gemcitabine**: given as a slow injection into the vein in a 28-day treatment cycle or as advised by the physician.
  - **Vinorelbine**: given as a slow injection into the vein as advised by the physician.



Participants received treatment until their cancer got worse, they had unacceptable side effects, or if they decided to leave the study. Participants were checked for side effects throughout the study.

To see if the cancer had spread, imaging scans were done once every 6 weeks for the first 54 weeks during the treatment period. Then, every 12 weeks for the rest of the treatment period. Researchers compared the scans done at the start and during the study. If a participant's scans showed that their cancer had grown, that meant their cancer had gotten worse.

Following the treatment period, participants entered a follow-up period 30 days after the last dose of treatment. This was done until the study ended, or the participant withdrew from the study. Researchers stayed in contact with participants to see how they were doing.

What were the results of the study?

This is a summary of the main results from this study. The individual results of each participant might be different and are not in this summary. A detailed presentation of the results can be found on the websites listed at the end of this summary.

How long did participants who got SG live without their cancer getting worse (known as progression-free survival or PFS) compared to participants who got chemotherapy?

Researchers wanted to find the PFS. PFS is the length of time from the beginning of the study until the participant's cancer had gotten worse, or they died.

The median length of time participants lived without their disease getting worse was recorded. Median is defined as the middle value of a list of values ordered from smallest to largest.

Participants treated with SG lived longer without their cancer getting worse compared to those who took chemotherapy. The median PFS time for both treatment groups is shown in the table below:

Progression-free survival time	
SG (out of 272 participants)	**Chemotherapy** (out of 271 participants)
5.5 months	4 months

Based on the difference in PFS between treatment groups, researchers found that in participants who received SG, the chances of their cancer getting worse were **35% less** than those who received chemotherapy.

Other results of the study

How long did participants who got SG live (known as overall survival or OS) compared to participants who got chemotherapy?

Researchers wanted to find how long participants lived from the start of the study until death. The overall survival for participants who received SG was 14.5 months. The overall survival for those who received chemotherapy was 11.2 months.

Researchers learned that participants treated with SG lived longer compared to those treated with chemotherapy.

What side effects did participants have during the study?

Unwanted medical events can happen to the study participants when they receive study treatments. In this summary, **side effects** are defined as unwanted medical events that the study doctors thought might be caused by the study treatment.

The results from several studies are usually needed to help decide if a treatment actually causes a side effect.

A side effect is considered **serious** if it:

- results in death
- is life-threatening
- considered by the study doctor to be medically important
- causes lasting problems
- requires hospital care
- causes a birth defect

26 participants did not take any study treatment. So, the results in this section only include 517 participants.

The table below shows how many participants had side effects during the study.

Overall side effects		
	SG (out of 268 participants)	**Chemotherapy** (out of 249 participants)
	Number of participants (%)	
How many participants had serious side effects?	36 (13%)	25 (10%)
How many participants had any side effects?	260 (97%)	217 (87%)
How many participants died from side effects?	1 (under 1%)	0
How many participants stopped taking study treatment because of side effects?	7 (3%)	9 (4%)

What were the serious side effects?

One participant in the SG group died from septic shock, a severe drop in blood pressure caused by an infection. This septic shock was caused by neutropenic colitis, where the large intestine is inflamed due to low levels of white blood cells in the blood.

Participants who received SG had more side effects like neutropenia and diarrhea, but overall these side effects were manageable with supportive treatments.

The table below shows the top 7 serious side effects that occurred in 1% or more of participants in either group. There were other serious side effects, but those occurred in fewer participants.

Serious side effects		
	SG (out of 268 participants)	**Chemotherapy** (out of 249 participants)
	Number of participants (%)	
Frequent loose watery stools (Diarrhea)	12 (4%)	1 (under 1%)
Fever with a low number of white blood cells (Febrile neutropenia)	11 (4%)	10 (4%)
Low number of white blood cells (Neutropenia)	8 (3%)	2 (under 1%)
Inflammation of the large intestine associated with low level of white blood cells called neutrophils in the blood (Neutropenic colitis)	5 (2%)	0
Vomiting	4 (1%)	2 (under 1%)
Inflammation of the large intestine (colitis)	4 (1%)	0
Feeling sick (Nausea)	2 (under 1%)	5 (2%)

What were the non-serious side effects?

The table below shows the top 5 most common non-serious side effects that occurred during the study. These side effects were not serious in nature and did not meet the definition of serious side effects mentioned in the section above in this summary.

There were other non-serious side effects, but those occurred in fewer participants. Some participants may have had more than 1 non-serious side effect.

Most common non-serious side effects		
	SG (out of 268 participants)	**Chemotherapy** (out of 249 participants)
	Number of participants (%)	
Low number of white blood cells (Neutropenia)	183 (68%)	132 (53%)
Frequent loose watery stools (Diarrhea)	149 (56%)	42 (17%)
Feeling sick to the stomach (Nausea)	148 (55%)	76 (31%)
Hair loss from part of the head or body (Alopecia)	123 (46%)	41 (16%)
Extreme tiredness (Fatigue)	102 (38%)	70 (28%)

How has this study helped researchers?

The researchers learned more about the safety of SG and how well it works compared to chemotherapy treatments of physician's choice in people living with HR+/HER2- metastatic breast cancer.

The results from several studies are needed to help decide which treatments work and are safe. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Gilead Sciences does plan to have further clinical studies with SG.

Where can I learn more about this study?

You can find more information about this study on the websites listed below.

Organization (Website)	Study Identifier
European Medicines Agency www.clinicaltrialsregister.eu	EudraCT Number: 2018-004201-33
United States National Institutes of Health (NIH) www.clinicaltrials.gov	ClinicalTrials.gov ID: NCT03901339
Gilead Clinical Trials www.gileadclinicaltrials.com	IMMU-132-09

Please note that information on these websites may be presented in a different way from this summary.

Full Study Title: Phase 3 Study of Sacituzumab Govitecan (IMMU-132) Versus Treatment of Physician's Choice (TPC) in Subjects With Hormonal Receptor-Positive (HR+) Human Epidermal Growth Factor Receptor 2 (HER2) Negative Metastatic Breast Cancer (MBC) Who Have Failed at Least Two Prior Chemotherapy Regimens

To learn more about clinical trials in general, please visit this page on www.clinicaltrials.gov website.

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Thank you

Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

GILEAD