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A Plain Language Summary of the ASCENT Study: Sacituzumab Govitecan for Metastatic Triple-Negative Breast Cancer

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Future ONCOLOGY

Plain Language Summary of Publication

A plain language summary of the ASCENT study: Sacituzumab Govitecan for metastatic triple-negative breast cancer

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Summary

Sacituzumab Govitecan (also known by the brand name TRODELVY®) is a new and available treatment for metastatic triple-negative breast cancer, or mTNBC for short. Metastatic breast cancer means the breast cancer has spread to other parts of the body. Triple negative means the breast cancer does not have 3 common proteins on the cell surface called receptors. This is a summary of the ASCENT study, published in the *New England Journal of Medicine* in April 2021. This study compared Sacituzumab Govitecan with standard chemotherapy. Chemotherapy is a treatment that kills cancer cells or stops them from dividing. 529 people with mTNBC took part in the study across 7 countries. All who took part had already received 2 previous chemotherapies, which stopped working for their cancer. The study showed that patients who took Sacituzumab Govitecan lived longer than those who took a different chemotherapy while on the study. Tumors shrank in more patients who took Sacituzumab Govitecan than in patients who took chemotherapy. In general, patients who took Sacituzumab Govitecan experienced more side effects. This included low levels of a type of white blood cell known as neutrophils (neutropenia) and loose or watery stool (diarrhea). Use of supportive care lessened these side effects. This summary also includes insights and perspectives from 2 breast cancer patient advocates.

How to say (double click to play sound).....

- **Sacituzumab Govitecan:** SAH-si-TOO-zoo-mab GOH-vih-TEE-kan
- **Antibody–drug conjugate:** AN-tee-BAH-dee-druhg-KON-jih-get
- **Capecitabine:** KAP-e-SYE-ta-been
- **Gemcitabine:** jem-SYE-ta-been
- **Vinorelbine:** vin-OR-el-been
- **Eribulin:** e-RIB-ue-lin

Who should read this article?

This summary may be helpful for patients and their caregivers, patient advocates, and healthcare professionals interested in new treatment options for metastatic triple-negative breast cancer. It will help them understand the results of this study. Two patient advocates co-authored this summary and added their perspectives.

Who sponsored this study?

This study was sponsored by Gilead Sciences, Inc.

Glossary

ADC: Antibody–drug conjugate
CT: Computed tomography
FDA: Food and Drug Administration
MRI: Magnetic resonance imaging
Trop-2: Trophoblast cell surface antigen 2

Future Medicine part of fsg

What is metastatic triple-negative breast cancer?

- **Breast cancer** is a disease where breast cells grow out of control and form a mass (tumor) that may spread to other parts of the body. This is also called metastasis, and the cancer is known as metastatic cancer.
- **Metastatic triple-negative breast cancer** is also known as **mTNBC**

mTNBC

m — **Metastatic**
Cancer that has spread to other parts of the body

TN — **Triple-Negative**
Cancer that first forms in the breast and does not have the estrogen receptor, progesterone receptor, and the HER2 protein on the surface of the cancer cells

BC — **Breast Cancer**

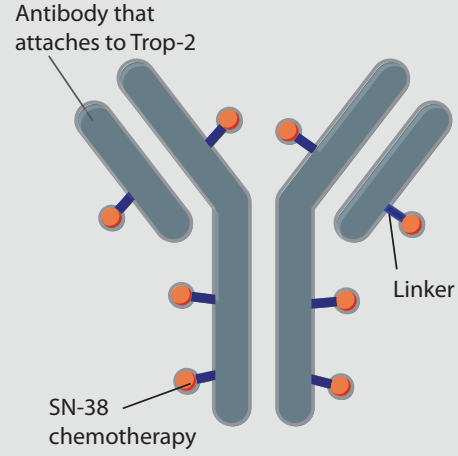
- There are 3 common proteins found on the surface of breast cancer cells. They are called receptors.
  - Estrogen receptor (also called ER)
  - Progesterone receptor (also called PR)
  - Human epidermal growth factor receptor 2 (also called HER2)
- All of these receptors are commonly measured in the laboratory as part of usual care for breast cancer.
- All of these receptors can affect how breast cancer cells grow.
- There are common breast cancer therapies for patients whose tumors are positive for these receptors.
  - Finding the right treatment for patients with TNBC is hard because hormone therapy or therapy that targets HER2 is not a good treatment option
  - Chemotherapy is currently the best treatment for patients with mTNBC. However, the breast cancer can come back after chemotherapy.
  - The patients of the ASCENT trials were adults with mTNBC that came back after chemotherapy.

What is an antibody–drug conjugate?

A common challenge in treating cancer is that some drugs kill cancer cells but may also kill healthy cells. This can lead to many side effects. Antibody–drug conjugates, also referred to as ADCs, are designed to treat only cancer cells. An ADC treats cancer by attaching to a receptor found only in cancer cells and delivering the chemotherapy directly in the cancer cell. This kills the cancer cells without killing healthy cells. This can lead to fewer side effects.

There are 3 components that make up Sacituzumab Govitecan, an ADC:

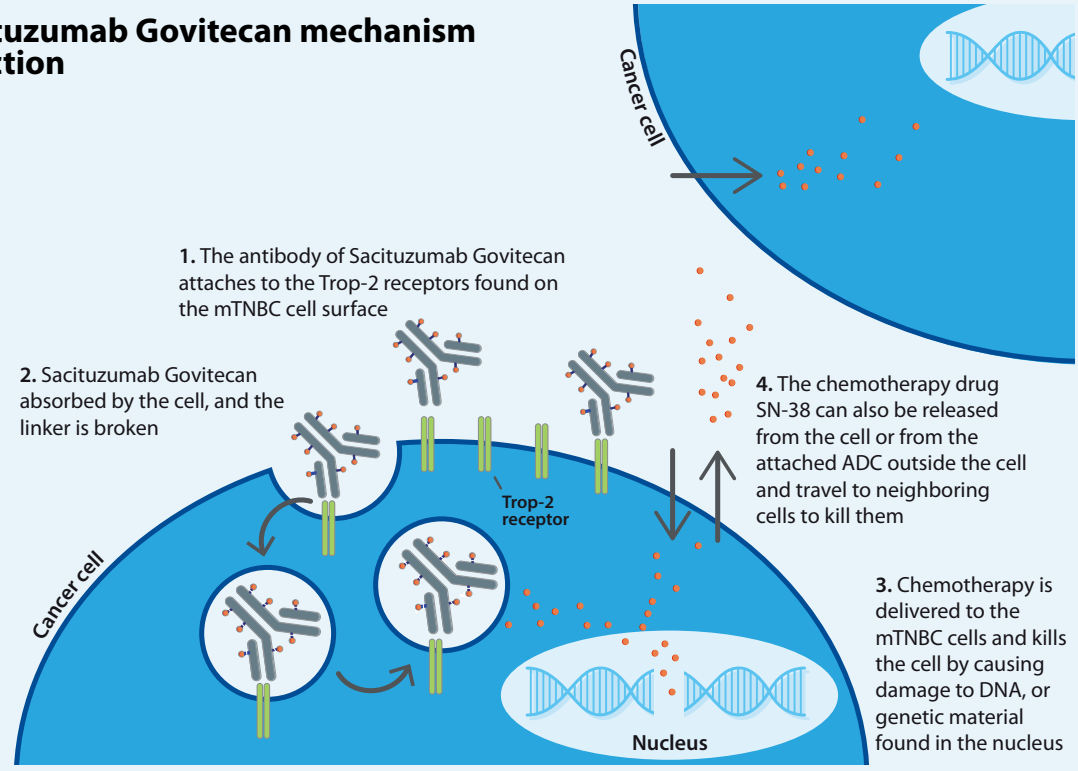
1. **An antibody (grey):** this is a protein that can find and attach to cancer cells (Trop-2)
2. **A chemotherapy drug (orange)**: this kills cancer cells (SN-38)
3. **A linker (dark blue)**: this connects the antibody to the chemotherapy drug, which breaks down to release the chemotherapy inside the cancer cell



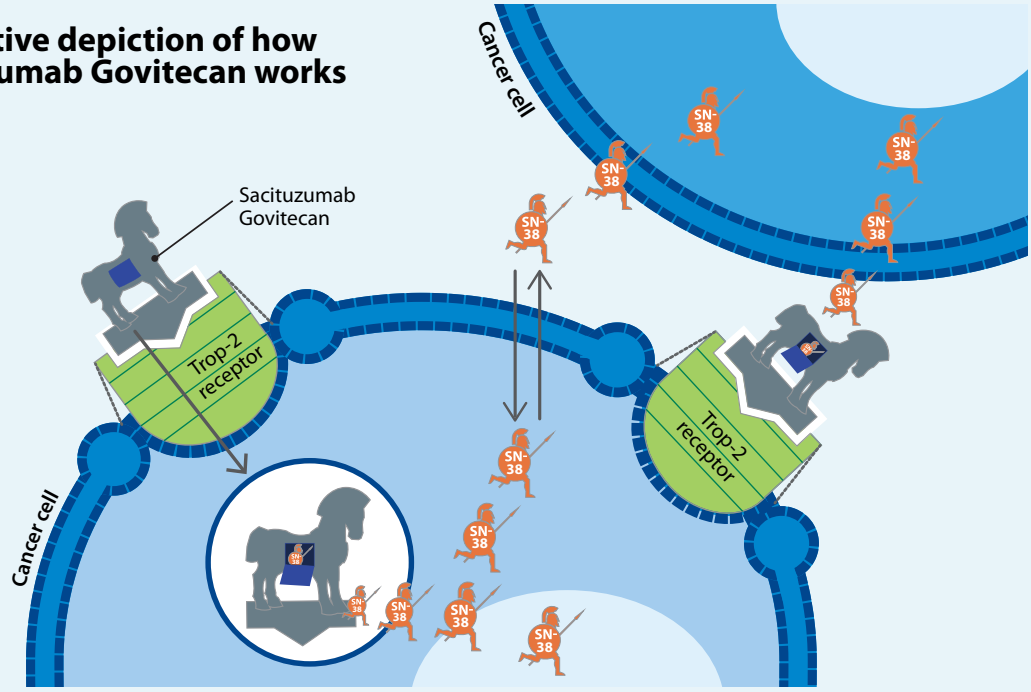
Sacituzumab Govitecan

Adapted from Rugo HS, *et al. Future Oncol.* (2020).

A. Sacituzumab Govitecan mechanism of action



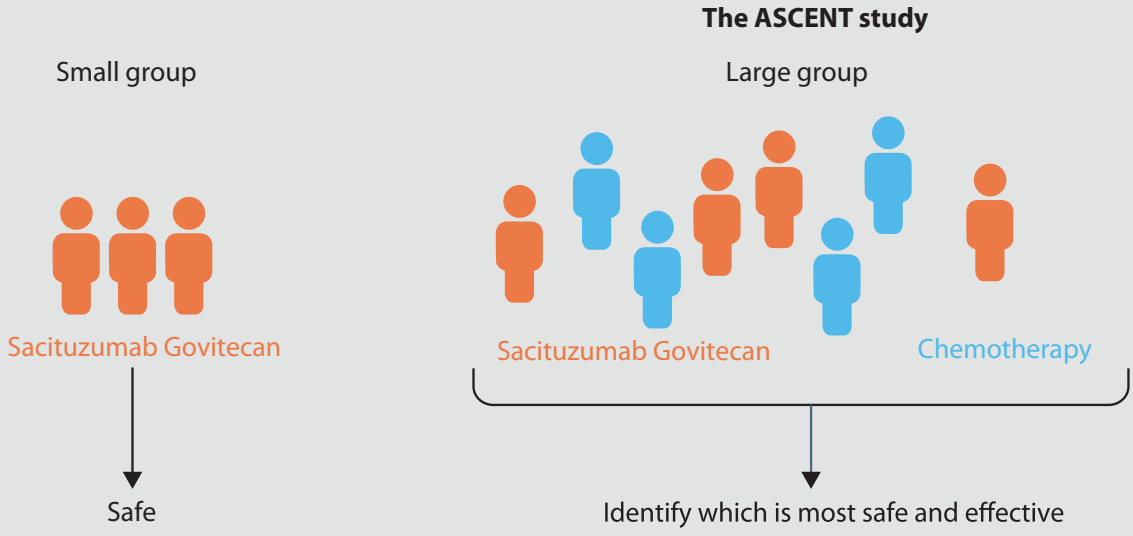
B. Illustrative depiction of how Sacituzumab Govitecan works



The Trojan horse analogy is utilized for simplicity and ease of understanding. In this analogy, the Trojan horse represents the antibody component of Sacituzumab Govitecan. The drawbridge represents the Trop-2 receptor, which helps the Trojan horse find cancer cells and enter them. Opening of the trapdoor, which represents the linker component of Sacituzumab Govitecan, allows the army of SN-38 chemotherapy (representing the payload component of Sacituzumab Govitecan) to attack cancer cells.
Adapted from Rugo HS *et al. Future Oncol.* (2020).

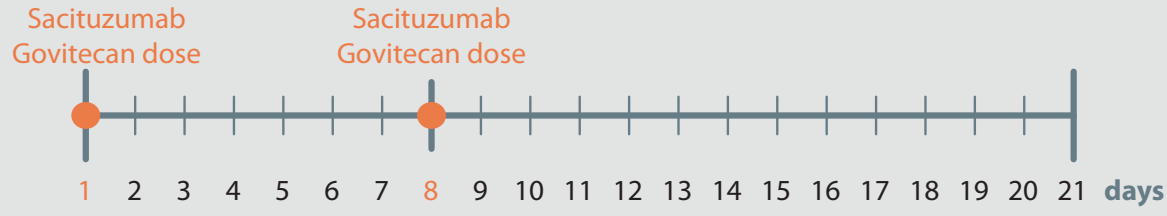
Why did the ASCENT study take place?

- There are not many treatments that work for patients with mTNBC.
- Sacituzumab Govitecan has been tested in a small number of patients with mTNBC. It was demonstrated to be safe and worked better than chemotherapy.
- The ASCENT study tested Sacituzumab Govitecan in a large number of patients who were randomly chosen to receive either Sacituzumab Govitecan or chemotherapy. The goal was to compare a new treatment (Sacituzumab Govitecan) with standard of care (chemotherapy) and thus identify the best and safest treatment for patients with mTNBC.



What happened in the ASCENT study?

- The ASCENT study began on November 7, 2017 and ended on March 11, 2020. A total of 529 patients with mTNBC (99.6% female; 2 males) enrolled in the ASCENT study.
- Patients were assigned by chance (also known as randomized) to Group A or Group B.
  - **Group A** received Sacituzumab Govitecan
  - **Group B** received chemotherapy chosen by the physician (either eribulin, vinorelbine, capecitabine, or gemcitabine)
- Sacituzumab Govitecan was given through an injection into the vein (also called intravenous or IV) on days 1 and 8 every 21 days.



Sacituzumab Govitecan treatment plan every 21 days

- Patients could withdraw from the study for the following reasons:
  - Their tumor grew or spread
  - Experienced unacceptable side effects
  - Voluntarily stopped treatment
  - Death
- 21 patients withdrew after treatment was started

Who took part in the ASCENT study?

Patients were able to take part in this study if they:

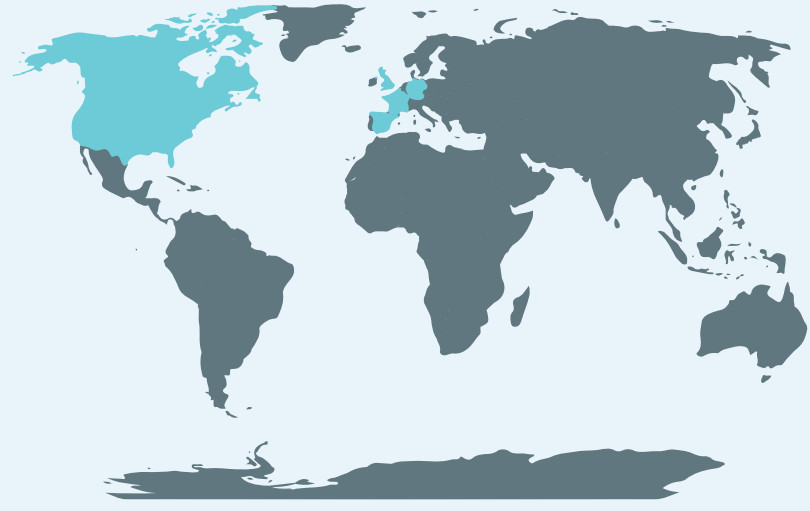
- ✓ Had mTNBC
- ✓ Either received at least 2 chemotherapies for mTNBC (1 had to be a taxane) that did not work well
- ✓ Or received at least 1 chemotherapy for mTNBC and received at least 1 chemotherapy given within 12 months of the cancer spreading to other parts of the body
- ✓ Were eligible for 1 of 4 chemotherapy options
- ✓ Had a tumor in the brain that stopped growing at least 4 weeks before taking part in this study (for those patients with cancer that spread to the brain [known as brain metastases])
- ✓ Had tumors that could be measured by computed tomography (also called CT) or magnetic resonance imaging (also known as MRI) scan

People were <u>not</u> able to take part in the study if they were:

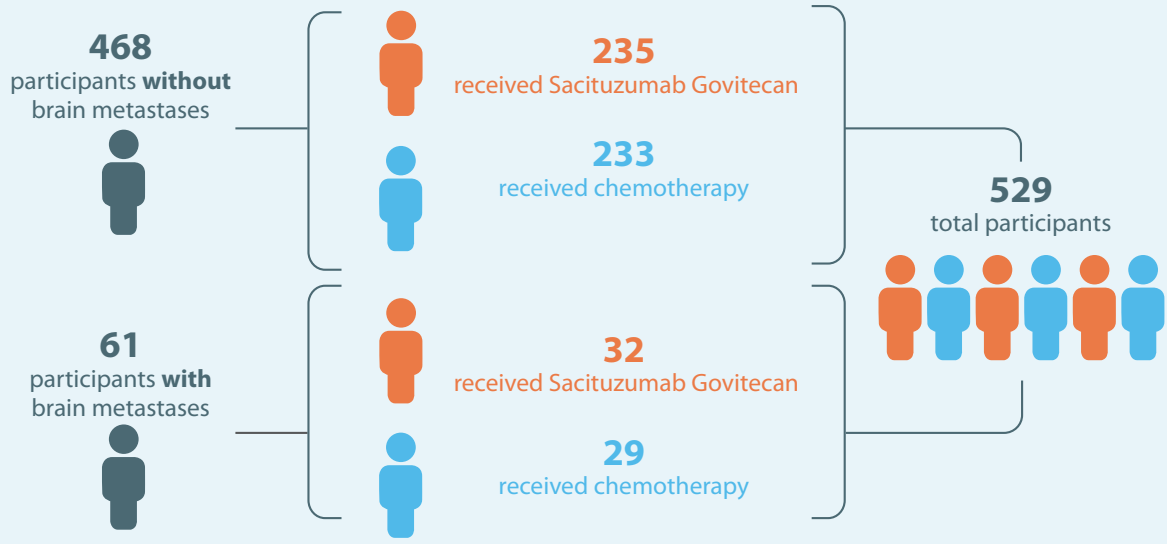
- ✕ Pregnant or breast-feeding
- ✕ Unwilling to use contraception (women of childbearing age or fertile men)
- ✕ Diagnosed with tumor(s) that spread only to the bone

The ASCENT study included patients from 7 countries:

Belgium Canada France
Germany Spain United States
United Kingdom



Here is a picture that explains the patients in this study:



What were the key questions answered in the study?

The key questions the ASCENT study researchers asked are as follows:

- In the patients without brain metastasis: How long did patients receiving Sacituzumab Govitecan live without their disease getting worse? **(main question)**
- In patients with and without brain metastasis: How long did patients receiving Sacituzumab Govitecan live without their disease getting worse?
- Did patients receiving Sacituzumab Govitecan live longer?
- Did tumor(s) get smaller in patients receiving Sacituzumab Govitecan?
- Is Sacituzumab Govitecan safe in a large number of patients?
- Did any patients receiving Sacituzumab Govitecan have any serious side effects caused by the treatment?

Please refer to the Educational resources section listed at the end of this summary to learn about the researcher's questions in the ASCENT study.

What were the overall results of the ASCENT study?

In April 2021, the ASCENT study group published their findings in the *New England Journal of Medicine*.

Please refer to the link at the end of the summary to read the full ASCENT study results.

Start of study
Who was included:

Adults with metastatic triple-negative breast cancer

who had at least 2 previous chemotherapies for advanced disease (1 had to be a taxane) that did not work well (or at least 1 chemotherapy for advanced disease, and 1 chemotherapy given before the advanced setting if the tumor grew within 12 months of this treatment)

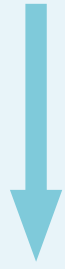
with tumors that could be measured by CT or MRI scan

Patients with known disease that spread to the brain were allowed in the study but the tumor had to have stopped growing for at least 4 weeks before the start of the study. Participants with disease that only spread to the bone were not allowed

Start of treatment

- 267 (50.5%) participants took Sacituzumab Govitecan
- 262 (49.5%) participants took chemotherapy

Treatment given until participant stopped responding or there were unacceptable side effects

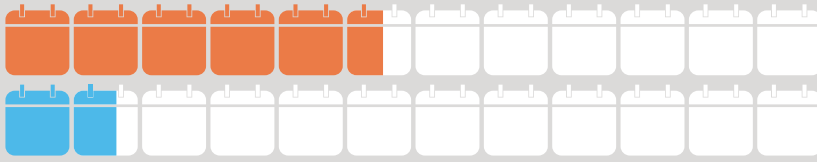


Key results
- Lived longer overall without their cancer getting worse
- Had more tumor(s) that shrank or disappeared
- Experienced more side effects like deceased white blood cells and loose or watery stool but were manageable with use of supportive treatments

How long did the patients live?

Length of time participants lived without their disease getting worse

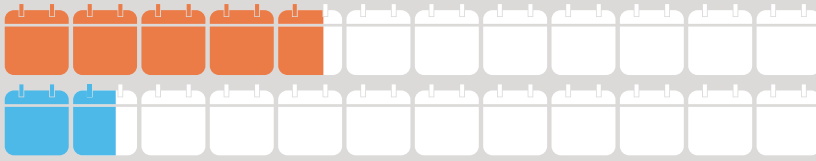
Participants without brain metastases



5.6 months
Group A (Sacituzumab Govitecan)
59% reduction in the chance of disease getting worse

1.7 months
Group B (chemotherapy)

Participants with or without brain metastases



4.8 months
Group A (Sacituzumab Govitecan)
59% reduction in the chance of disease getting worse

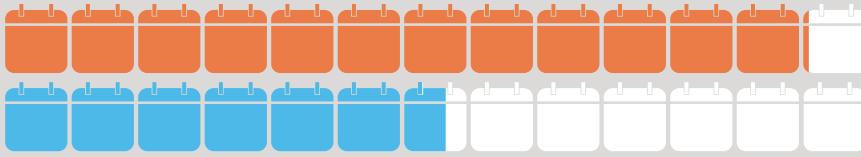
1.7 months
Group B (chemotherapy)

Patients who took Sacituzumab Govitecan lived longer without their disease getting worse compared with those who took chemotherapy.

The researchers reported the median (the middle value of a list of values ordered smallest to largest) length of time patients lived without their disease getting worse, also known as progression-free survival.

Length of survival time

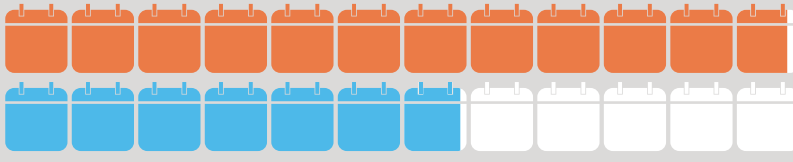
Participants without brain metastases



12.1 months
Group A (Sacituzumab Govitecan)
52% reduction in the chance of dying

6.7 months
Group B (chemotherapy)

Participants with or without brain metastases



11.8 months
Group A (Sacituzumab Govitecan)
49% reduction in the chance of dying

6.9 months
Group B (chemotherapy)

Patients who took Sacituzumab Govitecan lived longer compared with those who took chemotherapy.

The researchers reported the median length of time patients were still alive overall, also known as overall survival.

Tumor response

Percentage of participants with decrease in tumor size

Participants without brain metastases

35% (82 of 235)
Group A (Sacituzumab Govitecan)

5% (11 of 233)
Group B (chemotherapy)

Overall, more tumor(s) shrunk by at least 30% (partial response) or disappeared (complete response) in patients who took Sacituzumab Govitecan than those who took chemotherapy.

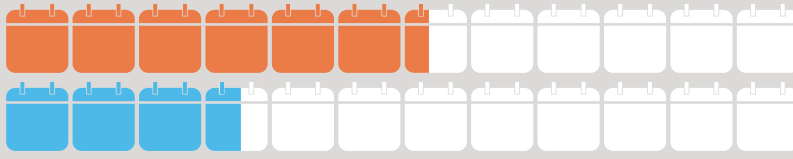
Participants with or without brain metastases

31% (83 of 267)
Group A (Sacituzumab Govitecan)

4% (11 of 262)
Group B (chemotherapy)

Length of time without tumor growth or spread

Participants without brain metastases

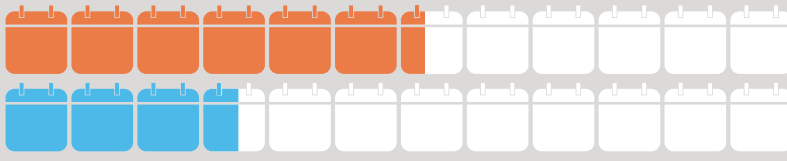


6.3 months
Group A (Sacituzumab Govitecan)

3.6 months
Group B (chemotherapy)

Tumors also stopped growing or spreading in the body for a longer length of time when treated with Sacituzumab Govitecan compared with chemotherapy. This is known as duration of response.

Participants with or without brain metastases



6.3 months
Group A (Sacituzumab Govitecan)

3.6 months
Group B (chemotherapy)

SAFETY

How many patients had side effects?

Percentage of participants with side effects:

Group A Sacituzumab Govitecan: **98%** (252 of 258 participants)

Group B chemotherapy: **86%** (192 of 224 participants)

Percentage of participants with treatment reduced:

Group A Sacituzumab Govitecan: **22%** (of 258 participants)

Group B chemotherapy: **26%** (of 224 participants)

Percentage of participants with treatment stopped:

Group A Sacituzumab Govitecan: **5%** (12 of 258 participants)

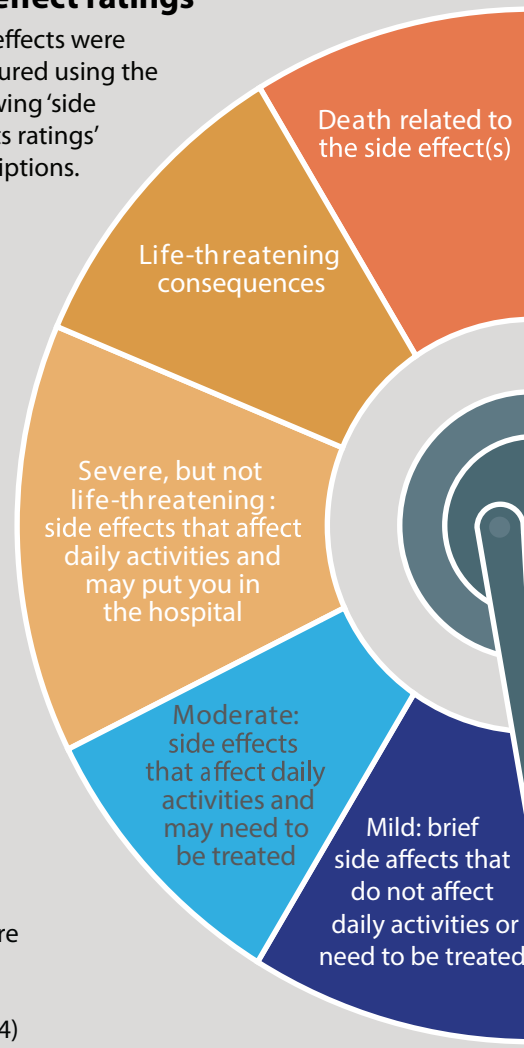
Group B chemotherapy: **5%** (12 of 224 participants)

This study monitored the safety of all patients who took at least 1 dose of their assigned drug:

- 258 patients took at least 1 dose of Sacituzumab Govitecan
- 224 patients took at least 1 dose of chemotherapy

Side effect ratings

- Side effects were measured using the following 'side effects ratings' descriptions.



What were the most common side effects?

Patients were monitored to see if Sacituzumab Govitecan caused more side effects compared with chemotherapy.
Some of the most common side effects are summarized here.

Sacituzumab Govitecan (out of 258) Chemotherapy (out of 224)

Neutropenia
(Low levels of neutrophils, a type of white blood cell)

63% (163)

43% (96)

Diarrhea
(Loose or watery stool)

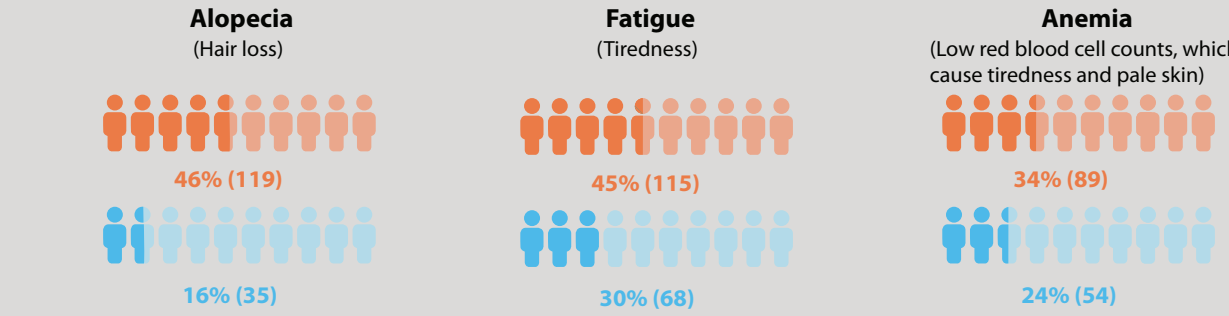
59% (153)

12% (27)

Nausea
(Feeling sick)

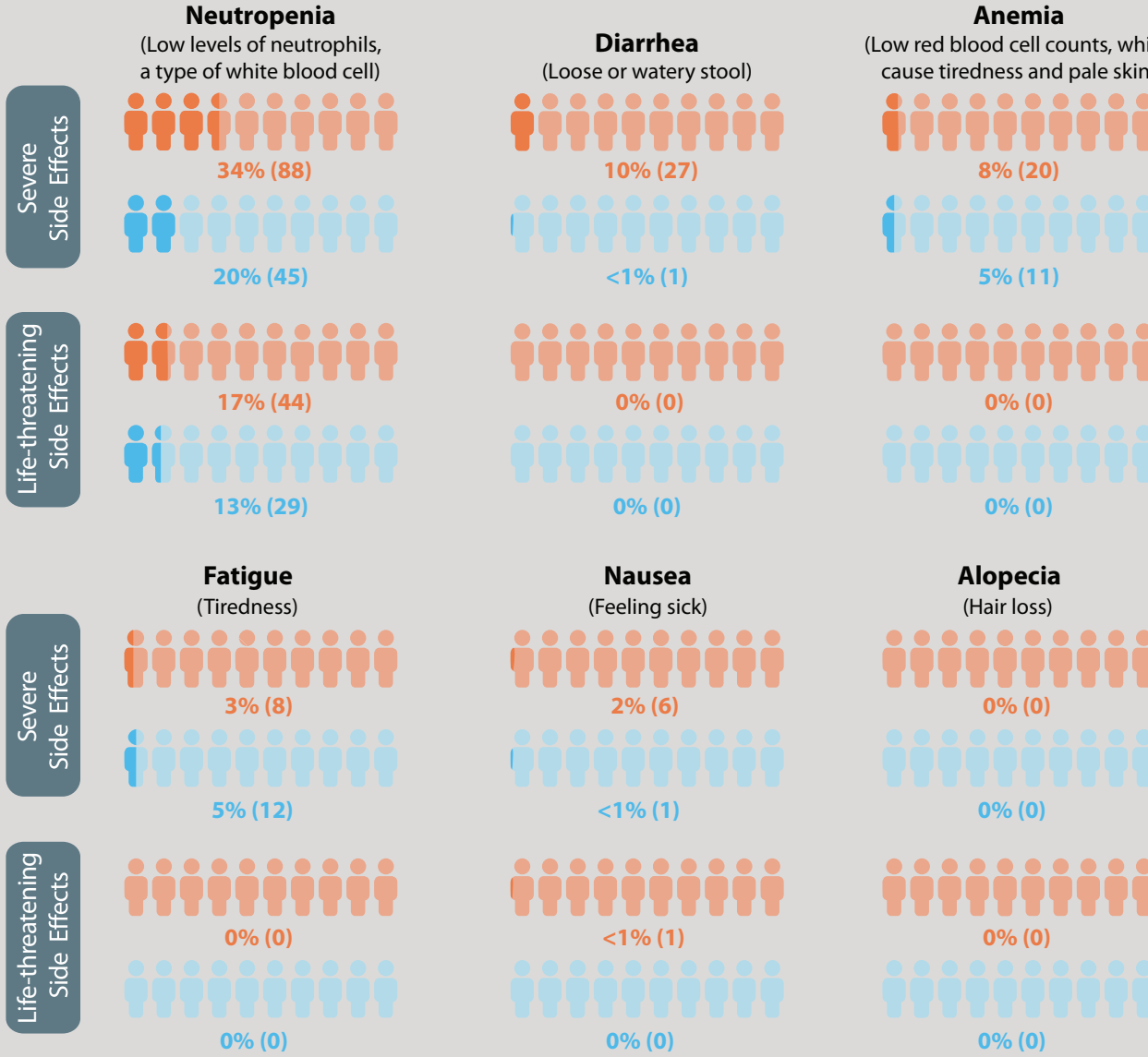
57% (147)

26% (59)



What were the most severe and life-threatening side effects?

The most severe and life-threatening side effects are summarized here. Other side effects (such as vomiting and stomach pain) were also mainly mild or moderate in both treatment groups.



How were side effects controlled in patients?

Neutropenia (low levels of neutrophils, a type of white blood cell) was controlled by decreasing the treatment dose or delaying treatment. The dose of treatment was decreased the same amount of times between the groups. Additionally, growth factors (natural substances that stimulate the bone marrow to make blood cells) may have been given to patients in both treatment groups to manage neutropenia.

For diarrhea, the recommendation was to immediately take an anti-diarrhea medication like loperamide (IMODIUM®) when the diarrhea started, until symptoms cleared.

Did any patients die because of treatment?

Side effects related to Sacituzumab Govitecan treatment did not cause any deaths. However, 3 patients in each group died. In the Sacituzumab Govitecan treatment group, 3 patients died from other causes like respiratory failure or a lung infection. In the chemotherapy treatment group, 1 patient died because of side effects from treatment, and the other 2 deaths were because of widespread infection and the disease getting worse.

What do the results of the ASCENT study mean?

Results from this study showed that of the patients with mTNBC without known brain metastases who took Sacituzumab Govitecan:

- 59% had a reduction in the chance of their disease getting worse,
- 52% had a reduction in the chance of dying,
- More tumors shrunk or disappeared, and
- Those with tumors that shrank tended to have a longer period of time without tumor growth.

Similar results were seen for the group of patients with and without known brain metastases. Although Sacituzumab Govitecan caused more side effects like neutropenia and diarrhea compared with chemotherapy, these side effects generally were mild to moderate and were manageable.

What does the ASCENT study mean for the patient community?

"Clinical trials advance science and are critical to the future of drug development for patients with cancer. As patients, by participating in these studies, we have the unique and exciting opportunity to participate in cutting-edge research and receive innovative treatments that may not be available otherwise.

When diagnosed with metastatic triple-negative breast cancer in 2016, my treatment options were limited to chemotherapy. The ASCENT study led to the development and approval of a brand-new treatment option for patients diagnosed with metastatic triple-negative breast cancer. Unlike chemotherapy, TRODELVY® finds the cancer cells, then releases the chemotherapy drug directly into those cells, sparing normal cells. The results of the ASCENT study demonstrated that patients who received TRODELVY® responded to treatment better and lived longer without their cancer spreading than those who only received chemotherapy.

As someone who is living with metastatic triple-negative breast cancer, this study offers me, and others who share this diagnosis, hope for our future. When standard chemotherapy fails, we now have another treatment option."

- Janice Cowden, Patient advocate living with stage IV metastatic triple-negative breast cancer

"Newly diagnosed patients with breast cancer dread the words "your tumor is triple negative." This means that some of the most effective treatments against breast cancer will not stop your cancer from growing. Triple negative breast cancer leads to worse outcomes in most patients. Researchers have spent years trying to find TNBC tumor markers for a new way to treat patients with TNBC.

The ASCENT study is important to patients. This study included patients who had already received multiple treatments for their cancer. It also included certain patients whose cancer had spread to their brain. Researchers can learn a lot about how this drug works in patients whose cancer has spread and in patients who have already had previous therapies.

This study provides hope to patients with metastatic triple negative breast cancer. It showed a new drug called Sacituzumab Govitecan might work against their cancer."

- Patty Spears, Patient advocate and breast cancer survivor

Where can readers find more information on the ASCENT study?

The original article discussed in this summary titled 'Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer' was published in the *New England Journal of Medicine* in 2021. You can read the abstract of the original article at: https://www.nejm.org/doi/full/10.1056/NEJMoa2028485

You can read more about the ASCENT study on the following websites:

- ClinicalTrials.gov (www.clinicaltrials.gov): type in the NCT number, NCT02574455 into the search bar to find the ASCENT study protocol or go to: https://clinicaltrials.gov/ct2/show/NCT02574455
- European Union Drug Regulating Authorities Clinical Trials Database (EudraCT) (https://eudract.ema.europa.eu/): type in the EudraCT number, 2017-003019-21 into the search bar to find the ASCENT study protocol or go to: https://www.clinicaltrialsregister.eu/ctr-search/search

If you were a study participant and have questions about the results of this trial and Sacituzumab Govitecan (brand name TRODELVY®), please speak with the physician or staff at your trial site.

Educational resources

Read more about metastatic triple-negative breast cancer on the Cancer.Net website at:
https://www.cancer.net/cancer-types/breast-cancer-metastatic/introduction

Read more about metastatic triple-negative breast cancer in the 2021 NCCN guidance for patients at:
https://www.nccn.org/patients/guidelines/content/PDF/stage_iv_breast-patient.pdf

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