Plain Language Clinical Study
Summary

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medicine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Seagen, Inc., a wholly owned subsidiary of Pfizer

Medicine(s) Studied: Ladiratuzumab Vedotin (LV; SGN-LIV1A)

Protocol Number: C5741001/SGNLVA-002

Dates of Study: 15 March 2018 to 15 October 2024

Title of this Study: Safety and Efficacy of SGN-LIV1A Plus Pembrolizumab for Patients With Locally-advanced or Metastatic Triple-Negative Breast Cancer

[Single Arm, Open Label Phase 1b/2 Study of SGN LIV1A in Combination With Pembrolizumab for First-Line Treatment of Patients With Unresectable Locally-Advanced or Metastatic Triple-Negative Breast Cancer]

Date(s) of this Report: 06 August 2025

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– Thank You –

If you participated in this study, Seagen Inc., a wholly owned subsidiary of Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. Do you have any questions about the study or the results? If so, please contact the doctor or staff at your study site.

Why was this study done?

What is triple-negative breast cancer?

Breast cancer is a disease where the cells in the breast grow out of control. There are different kinds of breast cancer depending on which cells grow out of control. In some types, the signal that triggers cell growth comes from hormones in the body, such as estrogen and progesterone. In other types of breast cancer, the signal that causes cells to grow faster is high levels of a protein called human epidermal growth factor receptor 2 (HER2). Triple-negative breast cancer (TNBC) is a type of breast cancer where the cancer cells don't have receptors for estrogen and progesterone and have no or a very low levels of HER2 proteins.

What is ladiratuzumab vedotin?

Ladiratuzumab vedotin (LV) is a type of drug called an antibody drug conjugate, or ADC. ADCs usually have 3 parts:

- Antibody: Antibodies are part of your immune system and usually help protect you from getting ill. In LV, the antibody part is designed to find and stick to the breast cancer cells in your body.
- Drug: The part of the ADC that kills cells. The cell-killing part of LV is a drug called monomethyl auristatin E, or MMAE.
- A “linker”: The “linker” attaches MMAE to the antibody, which allows MMAE to be released within target cancer cells.

LV is a new drug being investigated to help treat TNBC. At the time this study was run, LV was an investigational treatment. This means that it was not approved for use outside of research studies. LV is an “intravenous infusion” (IV) treatment, which means that a needle is placed in the vein and the drug slowly drips into the vein.

What is pembrolizumab?

Pembrolizumab (KEYTRUDA®) is an IV treatment approved for the treatment of certain types of cancer in the United States and some other countries. Pembrolizumab works by sticking to a protein called "anti-programmed cell death protein", which prevents it from protecting cancer cells from the body's immune system.

What was the purpose of this study?

- The purpose of this study was to learn about the safety of LV and pembrolizumab when used together, as well as how well they work against TNBC that has spread to other parts of the body.
- Researchers wanted to learn about the effects and "tolerability" of LV with pembrolizumab in participants with TNBC. "Tolerability" refers to how well participants can tolerate receiving the study treatment.
- Researchers wanted to find out the correct and best dose and dosing schedule of LV to use with pembrolizumab for treating participants with TNBC.
- As a part of the safety assessment in this study, researchers checked if participants treated with different doses of LV with pembrolizumab had any dose-limiting toxicities (DLTs). "DLTs" are certain medical problems caused by taking LV with pembrolizumab which require the participant to lower the dose or stop receiving the treatment (permanently or temporarily).

Researchers wanted to know:

- **What medical problems did participants have during the study?**
- **Did participants treated with different doses of LV and pembrolizumab have abnormal laboratory tests?**
- **Did participants treated with different doses of LV and pembrolizumab experience any DLTs?**
- **Did participants treated with different doses of LV with pembrolizumab have a reduction in tumor size?**

What happened during the study?

How was the study done?

This study consisted of Parts A, B, C, and D. Parts A and B are shown in Figure 1. Parts C and D are shown in Figure 2. This was an "open-label" study. This means researchers and participants knew what study medication participants received.

All participants were 'screened' before entering the 'treatment period' to see if they qualified to be in the study. Participants were treated with different doses of LV with pembrolizumab in "cycles". One (1) cycle was 21 days (3 weeks) in length. Participants were treated until their cancer got worse, they experienced unacceptable medical problems, they died, or they decided they wanted to stop receiving the study treatment.

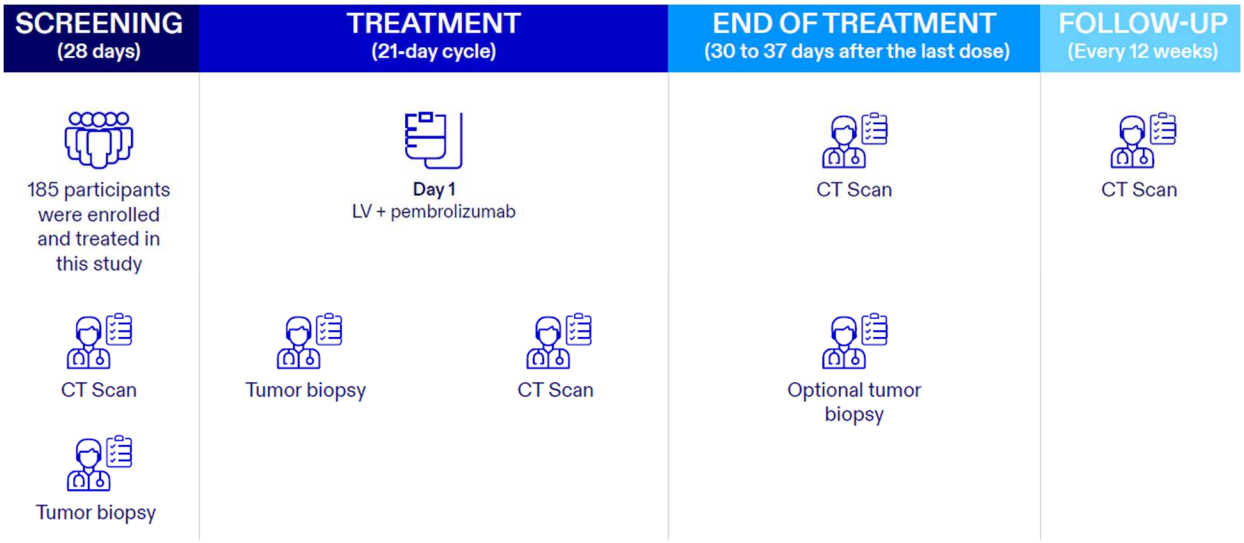
Part A

In Part A, participants were treated with LV 2.5 mg/kg every 3 weeks. The mg/kg is a unit to measure the drug dose. Participants were then treated with pembrolizumab 200 mg approximately 60 to 90 minutes after LV infusion completed.

Part B

Part B of this study was conducted in 2 groups. Participants enrolled first into Group 1 then into Group 2. Participants in Group 1 were treated with LV 2.5 mg/kg in combination with pembrolizumab. Participants in Group 2 were treated with LV 2.0 mg/kg, in combination with pembrolizumab. Participants in both groups were treated with LV and pembrolizumab every 3 weeks. Participants were treated with pembrolizumab 200 mg approximately 60 to 90 minutes after LV infusion completed.

Figure 1. Study plan (Part A and Part B)



Part C

In Part C, participants were treated with LV 1.0 or 1.25 mg/kg weekly on Day 1, Day 8, and Day 15 of every cycle. Participants were then treated with

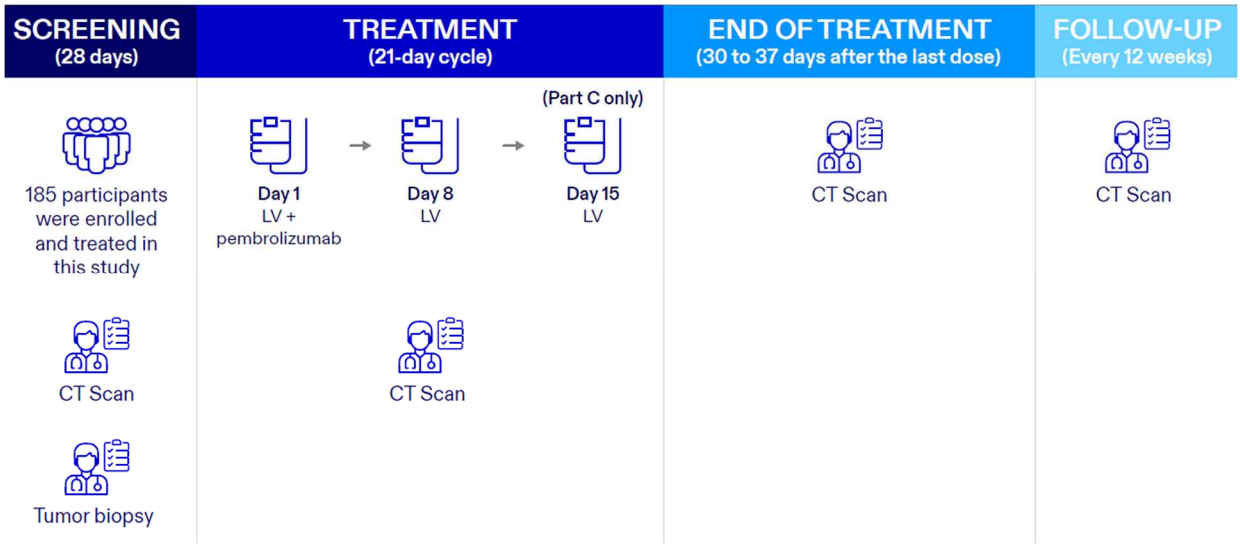
pembrolizumab 200 mg approximately 60 to 90 minutes after LV infusion completed on Day 1 of every 21-day cycle. Participants were first started on an LV dose of 1.0 mg/kg. Depending on the number of DLTs or other medical problems, participants were to be given an increased LV dose of 1.25 mg/kg.

Part D

In Part D, participants were treated with LV 1.5 mg/kg on Day 1 and Day 8 of every cycle. Participants were then treated with pembrolizumab 200 mg approximately 60 to 90 minutes after LV infusion completed on Day 1 of every cycle. Participants in Part D were not treated on Day 15.

Researchers assessed the safety and tolerability of different doses of LV with pembrolizumab by looking at the DLTs and medical problems participants had during the study. Researchers measured the effect of LV with pembrolizumab on participants' cancer by looking at the results of different tests of their tumors to assess the tumor growth before, during, and after treatment. These tests included a computed tomography scan, or "CT scan" which measures the size of tumors in the body. Researchers also tested tissue samples (called "biopsies") of participant's tumors. To do this, a small piece of the tumor was taken from participants and looked at. About 30 to 37 days after their last dose, all participants had an end of treatment visit where more tests, including CT scans were done. Participants then had CT scans every 12 weeks to assess their overall health, and to collect information on any additional treatment for their cancer. This is called 'follow-up'.

Figure 2. Study plan (Part C and Part D)



Where did this study take place?

The Sponsor ran this study at 35 locations in 4 countries in the United States, Spain, Germany, and South Korea.

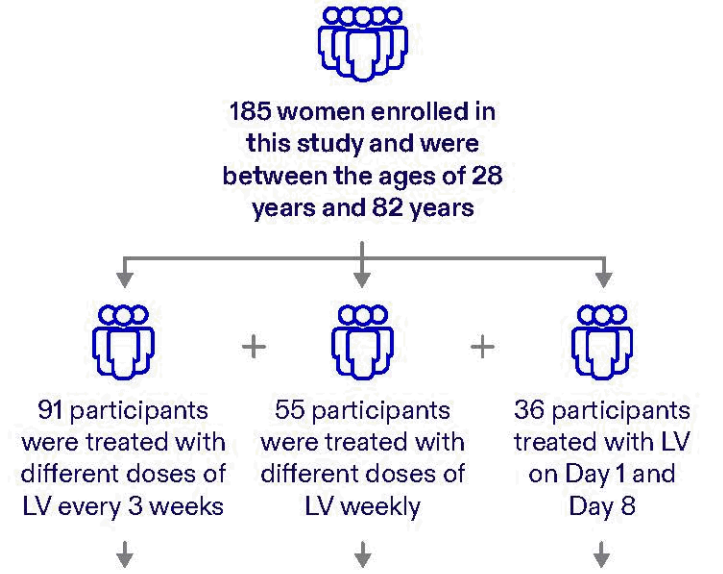
When did this study take place?

It began 15 March 2018 and ended 15 October 2024.

Who participated in this study?

The study included participants with TNBC that could not be removed by surgery. Figure 3 shows how many participants enrolled in the study, received the study treatments, and why they did not finish the study.

Figure 3. What happened to the participants during the study



	Participants did not finish the study for the following reasons:		
They no longer wanted to be in the study	8	4	3
The Sponsor ended the study	3	2	8
They were no longer able to be contacted after enrolling in the study for unknown reasons	7	4	2
They died	62	30	7
Other reasons	12	16	17

How long did the study last?

Participants were to be treated for around 2 years. The amount of time each participant was involved in the study varied. The entire study took approximately 6 years and 7 months to complete.

When the study ended in October 2024, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

Did participants treated with different doses of LV and pembrolizumab have abnormal laboratory tests?

Researchers looked at participants' laboratory tests results during the study to see if they changed during treatment. These tests looked at things like liver function, white blood cells, kidney function, and fat levels in the blood. The researchers did not find significant concerns with these test results.

Did participants treated with different doses of LV and pembrolizumab experience any DLTs?

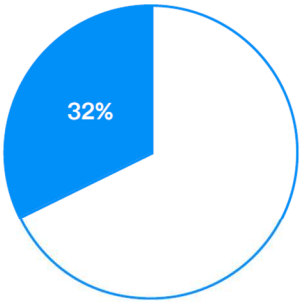
Two (2) out of 12 (17%) participants treated with LV 2.5 mg/kg and pembrolizumab every 3 weeks reported DLTs of large bowel inflammation and loose stools (diarrhea). No participants who received LV with pembrolizumab weekly reported a DLT.

Did participants treated with different doses of LV with pembrolizumab have a reduction in tumor size?

To answer this question, the researchers measured the "objective response rate" (ORR), which is the percentage of participants whose cancer got better (their tumor shrank or disappeared on images). Researchers measured the percentage of participants whose tumor shrank by 30% or more under treatment (called 'partial response') (Figure 4) and disappeared (called 'complete response') (Figure 5) after treatment.

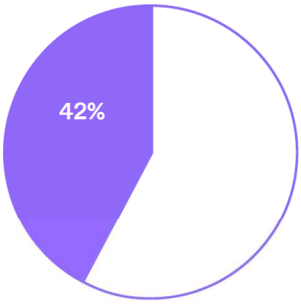
There were participants in each dosing schedule who showed a reduction in tumor size after being treated with different doses of LV with pembrolizumab. The ORR for each group is shown in Figure 6 below.

Figure 4. Number of participants who had a partial response



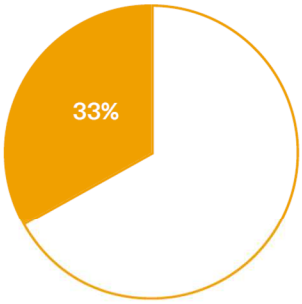
Participants treated every 3 weeks

29 out of 91 participants (32%) had a partial response



Participants treated weekly

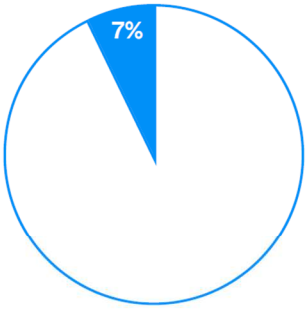
23 out of 55 participants (42%) had a partial response



Participants treated on Day 1 and Day 8

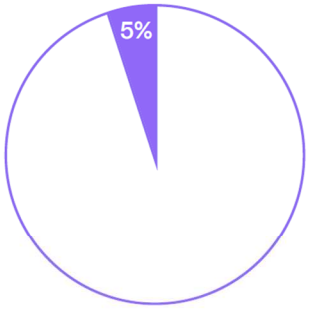
12 out of 36 participants (33%) had a partial response

Figure 5. Number of participants who had a complete response



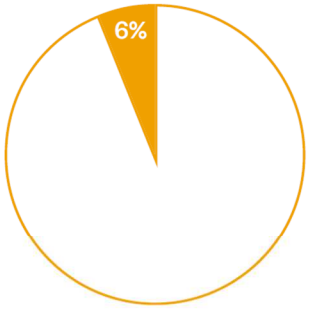
Participants treated every 3 weeks

6 out of 91 participants (7%) had a complete response



Participants treated weekly

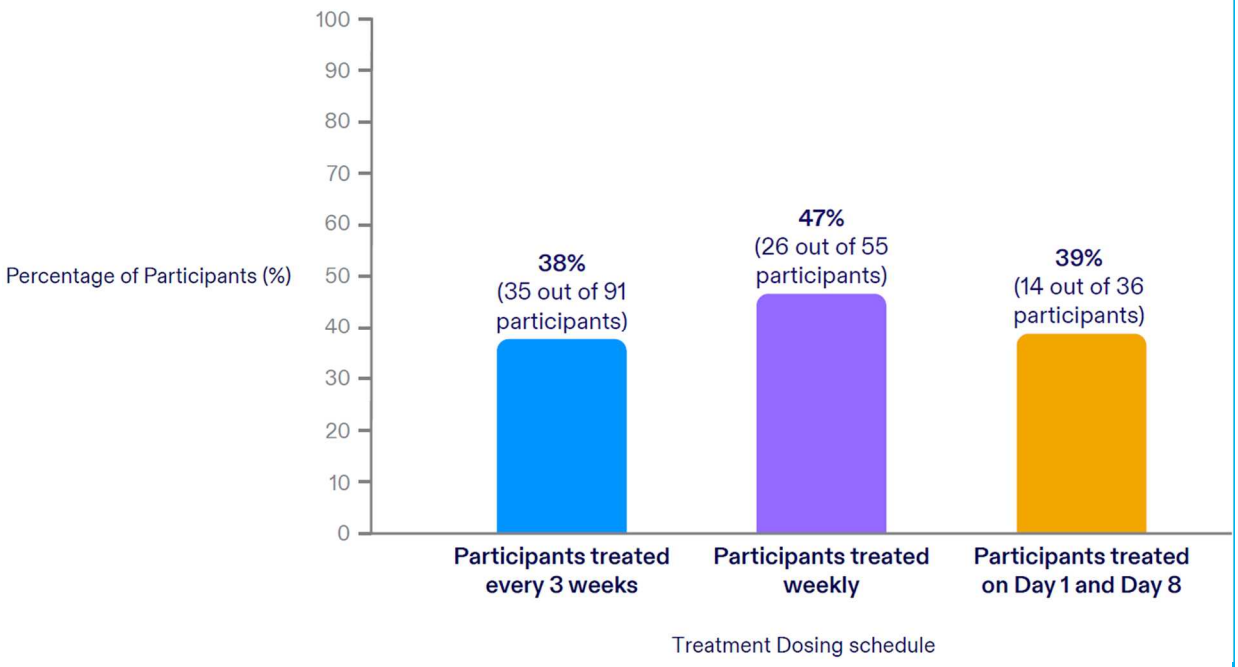
3 out of 55 participants (5%) had a complete response



Participants treated on Day 1 and Day 8

2 out of 36 participants (6%) had a complete response

Figure 6. Percentage of participants with reduction in tumor size



This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medicine might have on a participant.

All participants had at least 1 medical problem. A total of 15 participants (16%) treated every 3 weeks, 15 participants (27%) treated weekly, and 10 participants (28%) treated on Day 1 and Day 8 in every cycle discontinued from study treatment because of medical problems. The most common medical problems – those reported by more than 30% of participants – are described below.

Below are instructions on how to read Table 1, Table 2, and Table 3.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by more than 30% of participants treated every 3 weeks are listed.
- The **2nd** column tells how many of the 91 participants treated every 3 weeks reported each medical problem. Next to this number is the percentage of the 91 participants treated every 3 weeks and reported the medical problem.
- Using these instructions, you can see that 60 out of the 91 participants (66%) treated every 3 weeks reported feeling sick (nausea).

Instructions for Understanding Table 2.

- The **1st** column of Table 2 lists medical problems that were commonly reported during the study. All medical problems reported by more than 30% of participants treated weekly are listed.
- The **2nd** column tells how many of the 55 participants treated weekly reported each medical problem. Next to this number is the

percentage of the 55 participants treated weekly and reported the medical problem.

- Using these instructions, you can see that 35 out of the 55 participants (64%) treated weekly reported feeling tired (fatigue).

Instructions for Understanding Table 3.

- The **1st** column of Table 3 lists medical problems that were commonly reported during the study. All medical problems reported by more than 30% of participants treated on Day 1 and Day 8 in every cycle are listed.
- The **2nd** column tells how many of the 36 participants treated on Day 1 and Day 8 in every cycle reported each medical problem. Next to this number is the percentage of the 36 participants treated on Day 1 and Day 8 in every cycle and reported the medical problem.
- Using these instructions, you can see that 20 out of the 36 participants (56%) treated on Day 1 and Day 8 in every cycle reported feeling sick (nausea).

Table 1. Commonly reported medical problems by study participants treated every 3 weeks

Medical Problem	LV and Pembrolizumab (91 Participants)
Feeling sick (nausea)	60 out of 91 participants (66%)

Table 1. Commonly reported medical problems by study participants treated every 3 weeks	
Medical Problem	**LV and Pembrolizumab (91 Participants)**
Feeling tired (fatigue)	58 out of 91 participants (64%)
Loose stools (diarrhea)	45 out of 91 participants (49%)
Hair loss	44 out of 91 participants (48%)
Hard or dry stool	41 out of 91 participants (45%)
Sensory nerve damage in the limbs	37 out of 91 participants (41%)
Loss of appetite	36 out of 91 participants (40%)
Joint pain	29 out of 91 participants (32%)

Table 2. Commonly reported medical problems by study participants treated weekly	
Medical Problem	**LV and Pembrolizumab (55 Participants)**
Feeling tired (fatigue)	35 out of 55 participants (64%)
Feeling sick (nausea)	35 out of 55 participants (64%)
Loose stools (diarrhea)	31 out of 55 participants (56%)

Table 2. Commonly reported medical problems by study participants treated weekly	
Medical Problem	**LV and Pembrolizumab (55 Participants)**
Hard or dry stool	25 out of 55 participants (45%)
Increased level of a liver protein (enzyme) called "AST" in the blood	23 out of 55 participants (42%)
Sensory nerve damage in the limbs	20 out of 55 participants (36%)
Weight loss	20 out of 55 participants (36%)
Increased level of a liver protein (enzyme) called "ALT" in the blood	19 out of 55 participants (35%)
Loss of appetite	19 out of 55 participants (35%)
Stomach pain	18 out of 55 participants (33%)
Hair loss	18 out of 55 participants (33%)
Difficulty falling asleep	17 out of 55 participants (31%)
Vomiting	17 out of 55 participants (31%)

Table 3. Commonly reported medical problems by study participants treated on Day 1 and Day 8 in every cycle	
Medical Problem	**LV and Pembrolizumab (36 Participants)**
Feeling sick (nausea)	20 out of 36 participants (56%)
Loose stools (diarrhea)	16 out of 36 participants (44%)
Feeling tired (fatigue)	16 out of 36 participants (44%)
Sensory nerve damage in the limbs	13 out of 36 participants (36%)
Vomiting	13 out of 36 participants (36%)
Hair loss	12 out of 36 participants (33%)
Joint pain	12 out of 36 participants (33%)
Increased level of a liver protein (enzyme) called "AST" in the blood	12 out of 36 participants (33%)
Hard or dry stool	12 out of 36 participants (33%)
Low white blood cell count	12 out of 36 participants (33%)
Weight loss	11 out of 36 participants (31%)

Did study participants have any severe medical problems?

Researchers also looked at medical problems considered as severe or medically significant by the study doctors.

A total of 57 out of 91 (63%) participants treated every 3 weeks, 45 out of 55 (82%) participants treated weekly, and 26 out of 36 (72%)-participants treated on Day 1 and Day 8 in every cycle reported severe medical problems that were considered to be related to the study treatment.

Did study participants have any serious medical problems?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.

A total of 52 participants (57%) treated every 3 weeks, 29 participants (53%) treated weekly, and 14 participants (39%) treated on Day 1 and Day 8 in every cycle had serious medical problems. The most common serious medical problems – those reported by 4% or more of participants – are described below.

Below are instructions on how to read Table 4, Table 5, and Table 6.

Instructions for Understanding Table 4.

- The **1st** column of Table 4 lists serious medical problems that were commonly reported during the study. All serious medical problems reported by 4% or more of participants treated every 3 weeks are listed.
- The **2nd** column tells how many of the 91 participants treated every 3 weeks reported each serious medical problem. Next to this

number is the percentage of the 91 participants treated every 3 weeks and reported the serious medical problem.

- Using these instructions, you can see that 5 out of the 91 participants (5%) treated every 3 weeks reported headache.

Instructions for Understanding Table 5.

- The **1st** column of Table 5 lists serious medical problems that were commonly reported during the study. All serious medical problems reported by 4% or more of participants treated weekly are listed.
- The **2nd** column tells how many of the 55 participants treated weekly reported each serious medical problem. Next to this number is the percentage of the 55 participants treated weekly and reported the serious medical problem.
- Using these instructions, you can see that 4 out of the 55 participants (7%) treated weekly reported serious infection.

Instructions for Understanding Table 6.

- The **1st** column of Table 6 lists serious medical problems that were commonly reported during the study. All serious medical problems reported by 4% or more of participants treated on Day 1 and Day 8 in every cycle are listed.
- The **2nd** column tells how many of the 36 participants treated on Day 1 and Day 8 in every cycle reported each serious medical problem. Next to this number is the percentage of the 36 participants treated on Day 1 and Day 8 in every cycle and reported the serious medical problem.

- Using these instructions, you can see that 2 out of the 36 participants (6%) treated on Day 1 and Day 8 in every cycle reported large bowel inflammation.

Table 4. Commonly reported serious medical problems by study participants treated every 3 weeks

Serious Medical Problem	LV and Pembrolizumab (91 Participants)
Headache*	5 out of 91 participants (5%)
Stomach pain*	4 out of 91 participants (4%)
Sudden damage to the kidneys that causes them to not work properly*	4 out of 91 participants (4%)
Fluid on the lungs	4 out of 91 participants (4%)
Fever*	4 out of 91 participants (4%)
Vomiting*	4 out of 91 participants (4%)

*Researchers believed that these serious medical problems were related to the study treatment.

Table 5. Commonly reported serious medical problems by study participants treated weekly	
Serious Medical Problem	**LV and Pembrolizumab (55 Participants)**
Serious infection*	4 out of 55 participants (7%)
Sudden damage to the kidneys that causes them to not work properly*	3 out of 55 participants (5%)
Loose stools (diarrhea)*	3 out of 55 participants (5%)
Difficulty breathing	3 out of 55 participants (5%)
Stomach pain*	2 out of 55 participants (4%)
Low red blood cell count*	2 out of 55 participants (4%)
Loss of strength or energy*	2 out of 55 participants (4%)
Large bowel inflammation*	2 out of 55 participants (4%)
Blood clot in deep vein	2 out of 55 participants (4%)
Failure to thrive*	2 out of 55 participants (4%)
Feeling tired (fatigue)*	2 out of 55 participants (4%)
Muscle weakness*	2 out of 55 participants (4%)
Sensory nerve damage in the limbs*	2 out of 55 participants (4%)

Table 5. Commonly reported serious medical problems by study participants treated weekly	
Serious Medical Problem	**LV and Pembrolizumab (55 Participants)**
Lung blood clot	2 out of 55 participants (4%)
Fever*	2 out of 55 participants (4%)
Mouth pain and sores*	2 out of 55 participants (4%)
Infection of the kidneys, bladder, or urethra	2 out of 55 participants (4%)

*Researchers believed that these serious medical problems were related to the study treatment.

Table 6. Commonly reported serious medical problems by study participants treated on Day 1 and Day 8 in every cycle	
Serious Medical Problem	**LV and Pembrolizumab (36 Participants)**
Large bowel inflammation*	2 out of 36 participants (6%)
Low white blood cell count with fever*	2 out of 36 participants (6%)
Lung inflammation*	2 out of 36 participants (6%)

*Researchers believed that these serious medical problems were related to the study treatment.

A total of 62 participants, treated every 3 weeks, died during the study. Fifty-one (51) participants died due to disease under study, 3 participants died due to reasons unrelated to disease, and 8 participants died due to unknown cause. Researchers believe that 1 of these medical problems that led to death was related to study treatment.

A total of 30 participants, treated weekly, died during the study. Twenty-two (22) participants died due to disease under study, 4 participants died due to reasons unrelated to disease, and 4 participants died due to unknown cause. Researchers believe that 5 of these medical problems that led to death were related to study treatment.

A total of 7 participants, treated on Day 1 and Day 8 in every cycle died during the study. Three (3) participants died due to disease under study, 3 participants died due to reasons unrelated to disease, and 1 participant died due to unknown cause. Researchers believe that 2 of these medical problems that led to death were related to study treatment.

Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **C5741001/SGNLVA-002**

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT03310957**
https://euclinicaltrials.eu	Use the study identifier **2017-002289-35**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study,
thank you for volunteering.
We do research to try to find the best ways to help patients, and you helped us to do that!

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