Summary of the Results of the Clinical Trial for Laypersons

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 medication 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:	PF-08046046 (SGN-ALPV)
Protocol Number:	SGNALPV-001
EU Trial Number:	2022-500094-14-00
Clinical Trial Registry Identifier Number:	NCT05229900
Dates of Study:	21 April 2022 to 13 December 2023
Title of this Study:	A Study of SGN-ALPV in Advanced Solid Tumors [A Phase 1 Study of SGN-ALPV in Advanced Solid Tumors]
Date(s) of this Report:	11 July 2024

– 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 study was funded by Seagen, Inc., a wholly owned subsidiary of Pfizer, Bothell, WA, USA.

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

Why was this study done?

What are locally advanced or metastatic solid tumors?

Cancer occurs when cells in the body divide without control. Sometimes these cells form lumps called tumors. Locally advanced and metastatic solid tumors are tumors made up of cancer cells.

A locally advanced tumor is a tumor that has grown outside the body part it started in but has spread only to nearby organs or lymph nodes. A metastatic solid tumor is a tumor that started in one part of the body and spread to other distant parts of the body.

Participants in this study had locally advanced or metastatic solid tumors. They also had unresectable tumors, meaning it cannot be completely removed by surgery. The study included participants who had one of the following advanced or metastatic solid tumors:

- Ovarian cancer is a cancer that originates in the ovary (female reproductive organ).
- Non-small cell lung cancer is the most common type of lung cancer that starts when abnormal cells form and multiply in lung tissues.
- Cervical cancer is a cancer that starts in the cells of the cervix. Cervix is the lower part of the uterus that connects it to the vagina.
- Endometrial cancer is a cancer in the lining of the womb.
- Gastric and gastroesophageal junction (GEJ) cancer is a cancer of the stomach and the place where esophagus (tube connecting the throat to the stomach) is connected to the stomach.

- Malignant testicular germ cell tumor (GCT), except for pure teratomas, is a cancer that originates from cells in the testicles and later spread to other parts of the body. Teratomas is a type of tumor made of different tissues.
- Malignant ovarian GCT, except for pure teratomas, is a cancer that forms in the egg cells of the ovary and later spread to other parts of the body.
- Malignant extragonadal GCT with the exception of pure teratomas or tumors with primaries arising from the central nervous system. Extragonadal GCT can form in parts of the body other than the gonads (testicles or ovaries).

What is SGN-ALPV?

SGN-ALPV is an investigational medicine that is being developed to help treat advanced solid tumor cancer. An investigational medicine is one that is not approved for use outside of research studies.

SGN-ALPV is given as an infusion into a vein of the arm through a needle (intravenous or IV). It is a type of medicine called an “antibody drug conjugate”. An antibody drug conjugate is made up of an antibody with a toxic agent, which is chemically attached to it. Antibodies are proteins that can fight off infections and help prevent disease.

The antibody part of SGN-ALPV recognizes and sticks to specific proteins which are found in certain cancer cells. Researchers think that SGN-ALPV will deliver the toxic agent called MMAE directly to cancer cells, causing the cells to die.

What was the purpose of this study?

The purpose of this study was to learn about the safety and tolerability of SGN-ALPV in participants with solid tumors. "Tolerability" means how well participants can tolerate receiving the study medication.

- This was the first time SGN-ALPV was tested in humans. Researchers wanted to determine the recommended dose of the study medication. This would help them decide what dose to give to people in future studies.
- Researchers looked at whether participants had any "dose-limiting toxicities" (DLTs). These are medical problems that are severe and may have been caused by taking the study treatment at a dose that was probably too high. DLTs may mean that a participant had to stop taking the study treatment, either completely or for a short time.
- Researchers also evaluated the safety of the study treatment by recording the seriousness, type, frequency, and overall medical problems during the study.

Researchers wanted to know:

- How safe and well tolerated was SGN-ALPV?
    - Did participants have any medical problems considered to be DLTs?
    - Did participants in the study have medical problems that researchers believed were related to the study treatment?
    - Did participants in the study have any medical problems of Grade 3 or higher due to the study treatment?
    - Did participants in the study have any medical problems that led to discontinuation of study treatment?
- What medical problems did participants have during the study?

What happened during the study?

How was the study done?

First a study doctor checked each participant to make sure they were able to join the study based on the inclusion and exclusion criteria defined in the protocol. This is called “screening”.

Participants were then assigned to different treatment groups. The study design is shown in Figure 1, including treatment doses. The participants and researchers knew about what medication the participants received, and which dose. This is known as an “open-label” study.

Treatment was divided in blocks of 21 days called “cycles”. Participants received 2 doses of study medication on Day 1 and Day 8 of a 21-day cycle (also referred to as 2Q3W). Participants were treated in the study until their cancer got worse, they experienced unacceptable medical problems, they left before the study was over by their own choice, they started another therapy, the study doctor (investigator) decided it was best for a participant to stop taking the study treatment, or the Sponsor decided to end the study, whichever occurred first.

Participants received single increasing IV doses of SGN-ALPV starting from the lowest dose of 0.75 mg/kg as shown in Figure 1. For the first 4 participants, the dose was calculated based on their actual body weight. For the remaining participants, dose calculation was based on their adjusted ideal body weight (a measure used to calculate drug doses in study participants). SGN-ALPV 1.75 mg/kg was the highest dose tested in this study.

Participants visited their clinical site each cycle for checkups and study infusion treatments as necessary. If the participants experienced any

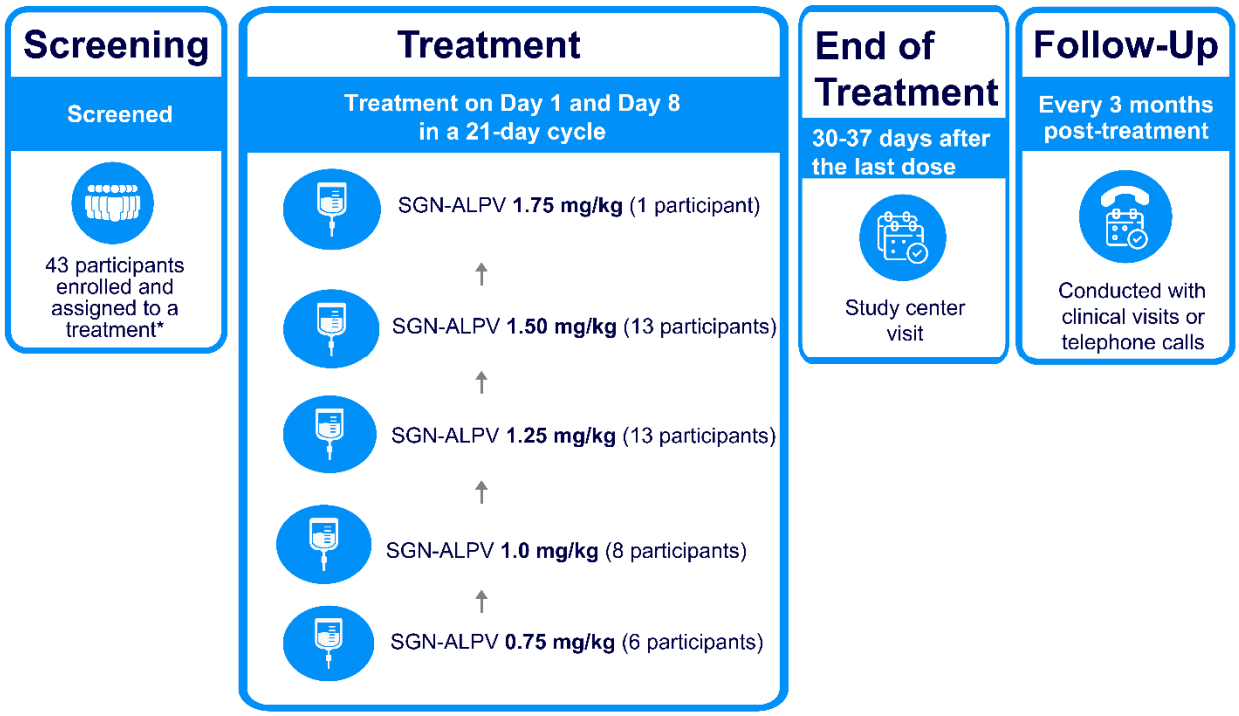
medical problems from the study medication, the dose of the medication was reduced, interrupted temporarily, or discontinued permanently.

Participants were to attend an “end of treatment” visit 30 to 37 days after their last dose of study treatment. Some participants were followed up by telephone or with clinical visits every 3 months after this visit.

Researchers took blood and tumor fragments from participants during the study and measured their tumor size. Researchers also checked the participants’ health during the study and asked them how they were feeling.

This is Part A of the study, also called as dose-escalation. Parts B and C of the study were initially planned but were not conducted by the Sponsor due to a business decision.

Figure 1. Study Plan



*43 participants enrolled and assigned to a treatment but only 41 participants were treated.

Where did this study take place?

The Sponsor ran this study at 11 locations in 5 countries in the United States of America, United Kingdom, Canada, Spain, and Sweden.

When did this study take place?

It began 21 April 2022 and ended 13 December 2023.

Who participated in this study?

Participants with one of the following metastatic or unresectable solid tumor types participated in this study:

- Ovarian cancer

- Non-small cell lung cancer
- Cervical cancer
- Endometrial cancer
- Gastric cancer and GEJ
- Malignant testicular GCT, except for pure teratomas
- Malignant ovarian GCT, except for pure teratomas
- Malignant extragonadal GCT with the exception of pure teratomas or tumors with primaries arising from the central nervous system

A total of 43 participants were enrolled in the study. Country wise enrollment of participants is shown in Figure 2.

Figure 2. Participants Enrollment by Country

Of the 43 participants enrolled 41 participants were treated with at least 1 dose of study treatment.

- A total of 9 men and 32 women participated.
- All participants were between the ages of 27 and 82 years.
- The study included 28 participants who were less than 65 years of age and 13 participants who were of 65 years of age or older.

All 41 participants stopped taking the study treatment. The 2 most common reasons were:

- Cancer got worse
- A medical problem

All 43 participants discontinued from the study because of these reasons:

- Death (22 participants)
- Sponsor closed the study (15 participants)
- Participants withdrew consent by their own choice (4 participants)
- Other (2 participants)

How long did the study last?

Study participants were in the study for varying lengths of time depending on how they responded to treatment. The entire study took 19 months and 23 days to complete.

The Sponsor ended the study in December 2023 due to a business decision. When the study ended, 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?

How safe and well tolerated was SGN-ALPV

The researchers assessed the safety and tolerability of SGN-ALPV by looking at the medical problems participants had during the study. They looked at the results of certain laboratory tests. Researchers recorded Grade 3 or higher medical problems reported during the study.

- Grade 3 medical problems are considered as the events to be severe or medically significant by the study doctors.
- Grade 4 medical problems are those considered as 'life-threatening' (could harm participants' health) and require urgent intervention by the study doctors.
- Grade 5 medical problems are those that result in death.

Medical problems throughout the whole of the study are discussed in full in the next section of this document.

Did participants have any medical problems considered to be DLTs?

One participant in the study had medical problems of sudden damage to the kidney and excessive breakdown of red blood cells causing tiredness and pale skin that researchers considered to be DLTs. This participant was in the SGN-ALPV 1.0 mg/kg treatment group.

There were no other DLTs reported for any other participants in the study.

Did participants in the study have medical problems that researchers believed were related to the study treatment?

Medical problems that researchers believed were related to the study treatment are shown in Figures 3, 4, 5, 6, and 7 by each study group. A total of 23 out of 41 (56%) participants experienced medical problems related to the study treatment.

Figure 3. Treatment Related Medical Problems in SGN-ALPV 0.75 mg/kg Group

SGN-ALPV 0.75 mg/kg group

1 out of 6 (17%) participants reported nerve damage causing difficulty with movements.

Figure 4. Treatment Related Medical Problems in SGN-ALPV 1.0 mg/kg Group

SGN-ALPV 1.0 mg/kg group

4 out of 8 (50%) participants reported medical problems related to the study treatment. Each event reported for 1 out 8 (13%) participants include:

- Nausea
- Feeling tired
- Sensory nerve damage to the limbs
- Low level of white blood cells called neutrophils
- High levels of blood sugar
- Sudden damage to the kidney
- High levels of creatinine (byproduct of muscle breakdown) in the blood
- Excessive breakdown of red blood cells causing tiredness and pale skin
- High blood levels of uric acid
- Low blood levels of potassium
- Muscle weakness
- Low level of white blood cells with fever due to infection
- Arm or leg pain
- Low level of "platelets" that help blood clot

Figure 5. Treatment Related Medical Problems in SGN-ALPV 1.25 mg/kg Group Reported by 2 or More Participants

SGN-ALPV 1.25 mg/kg group

9 out of 13 (69%) participants reported treatment related medical problems. The most common events were:

- Nausea, reported for 8 out of 13 (62%) participants
- Reaction to something given through a vein, reported for 4 out of 13 (31%) participants
- Feeling tired, hair loss
- Decreased appetite
- Diarrhea
- Fever
- Low blood pressure, each reported for 2 out of 13 (15%) participants

Figure 6. Treatment Related Medical Problems in SGN-ALPV 1.50 mg/kg Group Reported by 2 or More Participants

SGN-ALPV 1.50 mg/kg group

8 out of 13 (62%) participants reported treatment related medical problems.
The most common events were:

- Nausea, feeling tired, hair loss and increased liver test (aspartate aminotransferase) levels, each reported for 3 out of 13 (23%) participants
- Sensory nerve damage in the limbs, low level of white blood cells called neutrophils, vomiting, and increased liver test (alanine aminotransferase) levels, each reported for 2 out of 13 (15%) participants

Figure 7. Treatment Related Medical Problems in SGN-ALPV 1.75 mg/kg Group

SGN-ALPV 1.75 mg/kg group

Nausea, vomiting, high levels of blood sugar, and bad taste in mouth, reported for 1 out of 1 participant (100%) treated in this group.

Did participants in the study have any medical problems of Grade 3 or higher due to the study treatment?

All medical problems that were Grade 3 or higher and that researchers believed were related to study treatment are shown below, by treatment group. A total of 4 out of 41 (10%) participants reported Grade 3 or higher medical problems related to the study treatment.

SGN-ALPV 1.0 mg/kg Group

- Two out of 8 (25%) participants reported Grade 3 or higher medical problems related to the study treatment. These events were:
    - Sudden damage to the kidney, excessive breakdown of red blood cells causing tiredness and pale skin, high levels of blood sugar and uric acid, low level of white blood cells called neutrophils, low level of white blood cells with fever due to infection, and low level of "platelets" that help blood clot.

SGN-ALPV 1.50 mg/kg Group

- Two out of 13 (15%) participants reported Grade 3 or higher medical problems related to the study treatment. These events were:
    - Increased liver test (alanine and aspartate aminotransferase) levels and diarrhea.

There were no other Grade 3 or higher medical problems related to study treatment reported in other treatment groups in the study.

Did participants in the study have any medical problems that led to discontinuation of study treatment?

A total of 4 out of 41 (10%) participants had medical problems in different treatment groups as shown below, that led to discontinuation of study treatment.

- Increased liver test (alanine aminotransferase) levels, reported for 1 participant in **SGN-ALPV 1.50 mg/kg group**.

- Excessive breakdown of red blood cells causing tiredness and pale skin, reported for 1 participant in **SGN-ALPV 1.0 mg/kg group**.
- Reaction to something given through a vein, reported for 1 participant in **SGN-ALPV 1.25 mg/kg group**.
- Inflammation of heart muscle, reported for 1 participant in **SGN-ALPV 1.75 mg/kg group**.

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 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 medication might have on a participant.

Thirty-seven out of 41 (90%) participants in this study had at least 1 medical problem. A total of 4 participants left the study because of medical problems. The most common medical problems – those reported by 10% or more participants – are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The grey and white rows in Table 1 show individual medical problems that were commonly reported during the study. All medical problems reported by 10% or more participants are listed.

- The **1st** column of Table 1 tells how many of the 6 participants receiving SGN-ALPV 0.75 mg/kg reported each medical problem. Below this number is the percentage of the 6 participants receiving SGN-ALPV 0.75 mg/kg who reported the medical problem.

- The **2nd** column tells how many of the 8 participants receiving SGN-ALPV 1.0 mg/kg reported each medical problem. Below this number is the percentage of the 8 participants receiving SGN-ALPV 1.0 mg/kg who reported the medical problem.

- The **3rd** column tells how many of the 13 participants receiving SGN-ALPV 1.25 mg/kg reported each medical problem. Below this number is the percentage of the 13 participants receiving SGN-ALPV 1.25 mg/kg who reported the medical problem.

- The **4th** column tells how many of the 13 participants receiving SGN-ALPV 1.50 mg/kg reported each medical problem. Below this number is the percentage of the 13 participants receiving SGN-ALPV 1.50 mg/kg who reported the medical problem.

- The **5th** column tells if the 1 participant receiving SGN-ALPV 1.75 mg/kg reported each medical problem.

Below this number is the percentage of the 1 participant receiving SGN-ALPV 1.75 mg/kg who reported the medical problem.

- The **6th** column tells how many of the total (41) participants receiving SGN-ALPV reported each medical problem. Below this number is the percentage of the total participants who reported each medical problem.
- Using these instructions, you can see that:
  - One out of the 6 (17%) participants receiving SGN-ALPV 0.75 mg/kg reported nausea.
  - Two out of the 8 (25%) participants receiving SGN-ALPV 1.0 mg/kg reported nausea.
  - Eight out of the 13 (62%) participants receiving SGN-ALPV 1.25 mg/kg reported nausea.
  - Four out of the 13 (31%) participants receiving SGN-ALPV 1.50 mg/kg reported nausea.
  - One out of the 1 (100%) participant receiving SGN-ALPV 1.75 mg/kg reported nausea.
  - A total of 16 out of 41 (39%) participants reported nausea in the study.

Table 1. Commonly reported medical problems reported by 10% or more study participants					
SGN-ALPV					
0.75 mg/kg (6 participants)	**1.0 mg/kg** (8 participants)	**1.25 mg/kg** (13 participants)	**1.50 mg/kg** (13 participants)	**1.75 mg/kg** (1 participant)	**Total** (41 participants)
Nausea					
1 out of 6 participants (17%)	2 out of 8 participants (25%)	8 out of 13 participants (62%)	4 out of 13 participants (31%)	1 out of 1 participant (100%)	16 out of 41 participants (39%)
Feeling tired					
0	1 out of 8 participants (13%)	4 out of 13 participants (31%)	3 out of 13 participants (23%)	1 out of 1 participant (100%)	9 out of 41 participants (22%)
Hair loss					
0	0	2 out of 13 participants (15%)	4 out of 13 participants (31%)	0	6 out of 41 participants (15%)
Shortness of breath					
1 out of 6 participants (17%)	0	2 out of 13 participants (15%)	2 out of 13 participants (15%)	1 out of 1 participant (100%)	6 out of 41 participants (15%)
Low levels of blood potassium					
2 out of 6 participants (33%)	1 out of 8 participants (13%)	2 out of 13 participants (15%)	1 out of 13 participants (8%)	0	6 out of 41 participants (15%)
Vomiting					
0	2 out of 8 participants (25%)	1 out of 13 participants (8%)	2 out of 13 participants (15%)	1 out of 1 participant (100%)	6 out of 41 participants (15%)

Table 1. Commonly reported medical problems reported by 10% or more study participants					
SGN-ALPV					
0.75 mg/kg (6 participants)	**1.0 mg/kg** (8 participants)	**1.25 mg/kg** (13 participants)	**1.50 mg/kg** (13 participants)	**1.75 mg/kg** (1 participant)	**Total** (41 participants)
Low level of red blood cells					
1 out of 6 participants (17%)	0	2 out of 13 participants (15%)	2 out of 13 participants (15%)	0	5 out of 41 participants (12%)
Increased liver test (aspartate aminotransferase) levels					
0	0	2 out of 13 participants (15%)	3 out of 13 participants (23%)	0	5 out of 41 participants (12%)
Feeling less hungry					
0	0	2 out of 13 participants (15%)	2 out of 13 participants (15%)	0	4 out of 41 participants (10%)
Diarrhea					
0	0	3 out of 13 participants (23%)	1 out of 13 participants (8%)	0	4 out of 41 participants (10%)
Headache					
0	0	2 out of 13 participants (15%)	2 out of 13 participants (15%)	0	4 out of 41 participants (10%)
Reaction to something given through a vein					
0	0	4 out of 13 participants (31%)	0	0	4 out of 41 participants (10%)
Low level of white blood cells called neutrophils					

Table 1. Commonly reported medical problems reported by 10% or more study participants					
SGN-ALPV					
0.75 mg/kg (6 participants)	**1.0 mg/kg** (8 participants)	**1.25 mg/kg** (13 participants)	**1.50 mg/kg** (13 participants)	**1.75 mg/kg** (1 participant)	**Total** (41 participants)
0	1 out of 8 participants (13%)	1 out of 13 participants (8%)	2 out of 13 participants (15%)	0	4 out of 41 participants (10%)
Numbness in the limbs					
0	1 out of 8 participants (13%)	1 out of 13 participants (8%)	2 out of 13 participants (15%)	0	4 out of 41 participants (10%)
Fever					
0	1 out of 8 participants (13%)	2 out of 13 participants (15%)	1 out of 13 participants (8%)	0	4 out of 41 participants (10%)

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 12 out of 41 (29%) participants had serious medical problems, of which 3 participants (7%) had serious medical problems related to the study treatment. The most commonly reported serious medical problems were:

- Blockage in the bowel blood vessels (3 participants)
- Clot in a blood vessel in the lung (2 participants)

Serious medical problems related to the study treatment were:

- Sudden damage to the kidney, excessive breakdown of red blood cells causing tiredness and pale skin, and low level of white blood cells with fever due to infection, reported for 1 participant each in SGN-ALPV 1.0 mg/kg group.
- Increased liver test (alanine and aspartate aminotransferase) levels, and fever, reported for 1 participant each in SGN-ALPV 1.50 mg/kg group.

A total of 22 participants died during the study. One participant died during the treatment period (within 30 days after the last dose of SGN-ALPV) due to excessive breakdown of red blood cells. Fifteen participants died due to disease under the study and the reason for the death of 6 participants is unknown.

How has this study helped participants and researchers?

This study provided participants with a potential treatment option after trying all standard of care options. While no objective responses (best overall response of disappearance of disease after treatment) were observed, some participants did experience prolonged stable disease (cancer had neither increased nor decreased in extent or severity). As with any first in human study, the benefit to participants may be limited, given the nature of these studies that evaluate an investigational medicine for the first time in humans.

Are there any plans for further studies?

At this time there are no plans for further studies.

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 SGNALPV-001

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

www.clinicaltrials.gov	Use the study identifier **NCT05229900**
www.clinicaltrialsregister.eu	Use the study identifier 2022-500094-14-00

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!