NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about LAG525 given together with spartalizumab, or with spartalizumab and carboplatin, or with carboplatin, in people with advanced triple-negative breast cancer

Protocol number: CLAG525B2101

Thank You!

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public.

Thanks to participants for taking part in this trial for the drug LAG525. They helped researchers learn more about how LAG525 works in people with triple-negative breast cancer (TNBC).

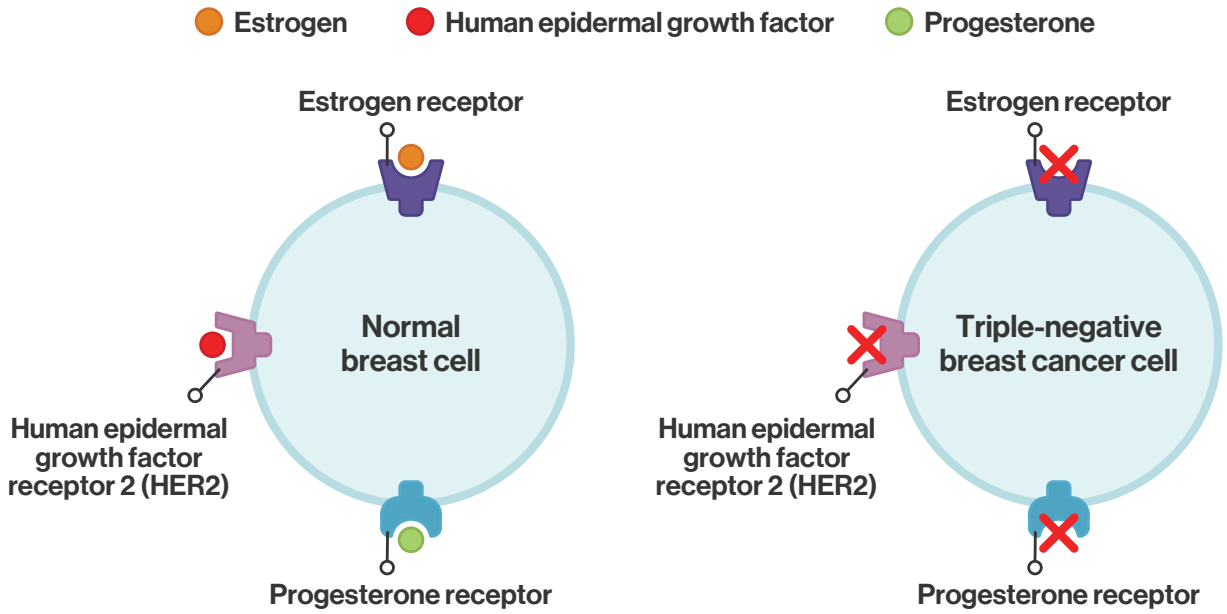
If there are any questions about the trial results, please talk to the doctor or staff at the trial site.
The summary shows the results of a single clinical trial. Other clinical trials may have different findings.

Why was the research needed?

Researchers were looking for a better way to treat advanced triple-negative breast cancer (TNBC). TNBC is an aggressive type of breast cancer that grows without having any of the three receptors that are usually found in other types of breast cancer. This makes it harder for doctors to know how the cancer may spread and what treatments might work best. TNBC is a serious and life-threatening cancer which currently has no cure.

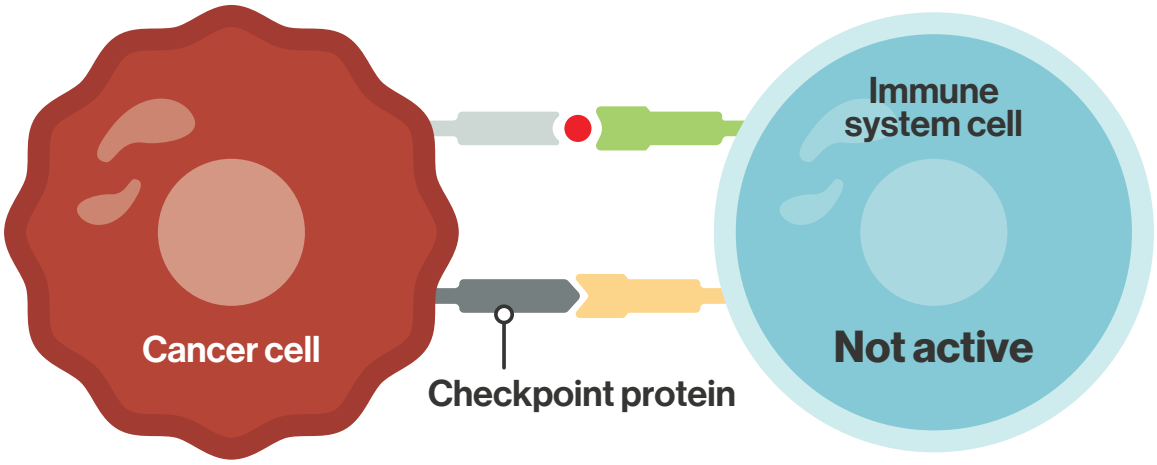
Receptors are proteins that live inside or on the surface of a cancer cell and bind to specific substances causing the cancer cell to grow. Most breast cancers have receptors for estrogen, progesterone, or human epidermal growth factor receptor 2 (HER2).

Receptors in a normal breast cell vs a cell with triple-negative breast cancer (TNBC)

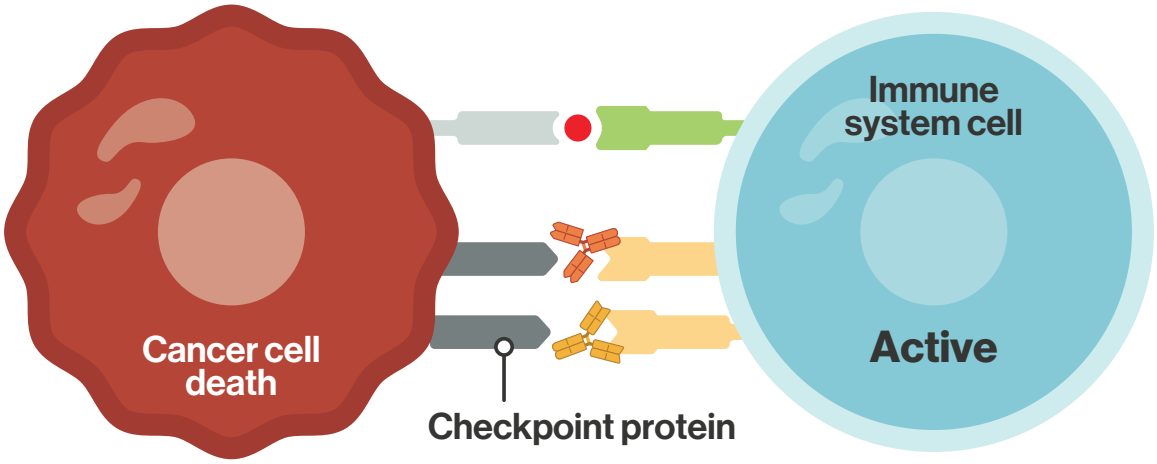


Chemotherapy is frequently the only treatment of choice for patients with TNBC. Chemotherapy drugs such as carboplatin weaken or destroy cancer and normal cells by damaging the genetic material in the cells, thereby making it difficult for the cancer cells to continue living. However, even if the cancer shrinks or disappears, it can often return in many of these patients, progressing rapidly and leading to a lower percentage of patients who lived after treatment (survival rate).

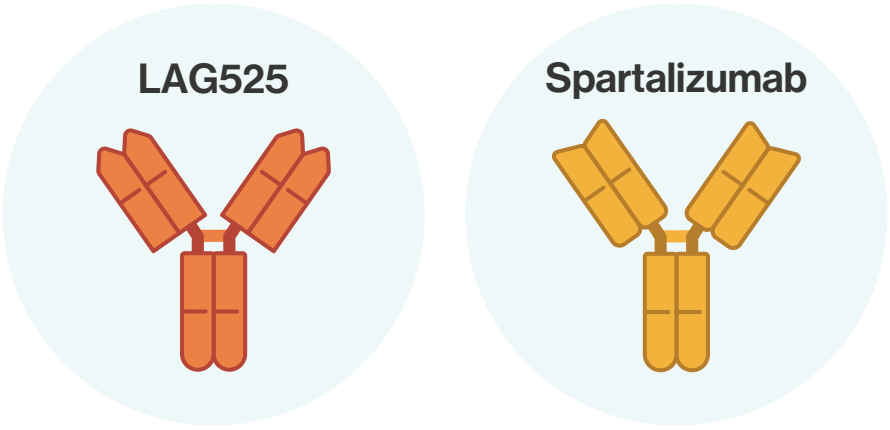
Another way to help fight cancer is by boosting (activating) the patient's immune system. One group of drugs that can do this are called immune checkpoint inhibitors; these drugs block a group of proteins called "checkpoints." Checkpoint proteins are made by a person's immune system, as well as some cancer cells, and can prevent the immune system from killing cancer cells. Checkpoint inhibitors such as LAG525 and spartalizumab work by helping the immune system kill cancer cells easier.



Checkpoint proteins prevent the immune system from killing cancer cells.



Checkpoint inhibitors such as LAG525 and spartalizumab help the immune system to kill cancer cells easier.



Researchers have shown that using a combination of checkpoint inhibitors could have a better anti-cancer effect than using a single one. Researchers have also found that using a combination of chemotherapy drugs and checkpoint inhibitors together can be more effective in managing cancer than using each drug group separately.

Trial drug

The treatments in this trial were:

1. LAG525, which was used to inhibit a checkpoint protein on the cancer cell
2. Spartalizumab, which was also used to inhibit a checkpoint protein on the cancer cell. This drug is currently approved for the treatment of another type of cancer.
3. Carboplatin, a chemotherapy medication currently approved for the treatment of cancers, specifically triple-negative breast cancer.

All drugs were administered through the vein into the bloodstream (IV infusion).

Trial purpose

In this trial, researchers wanted to learn more about the effectiveness and safety of LAG525 in patients with advanced triple-negative breast cancer, when given together with:

- spartalizumab, or
- spartalizumab and carboplatin, or
- carboplatin

How long was this trial?

The trial started in July 2018 and ended in November 2021. The entire duration, from enrolling the first participant to the last participant completing the trial was around 3 years.

When the trial ended, the researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

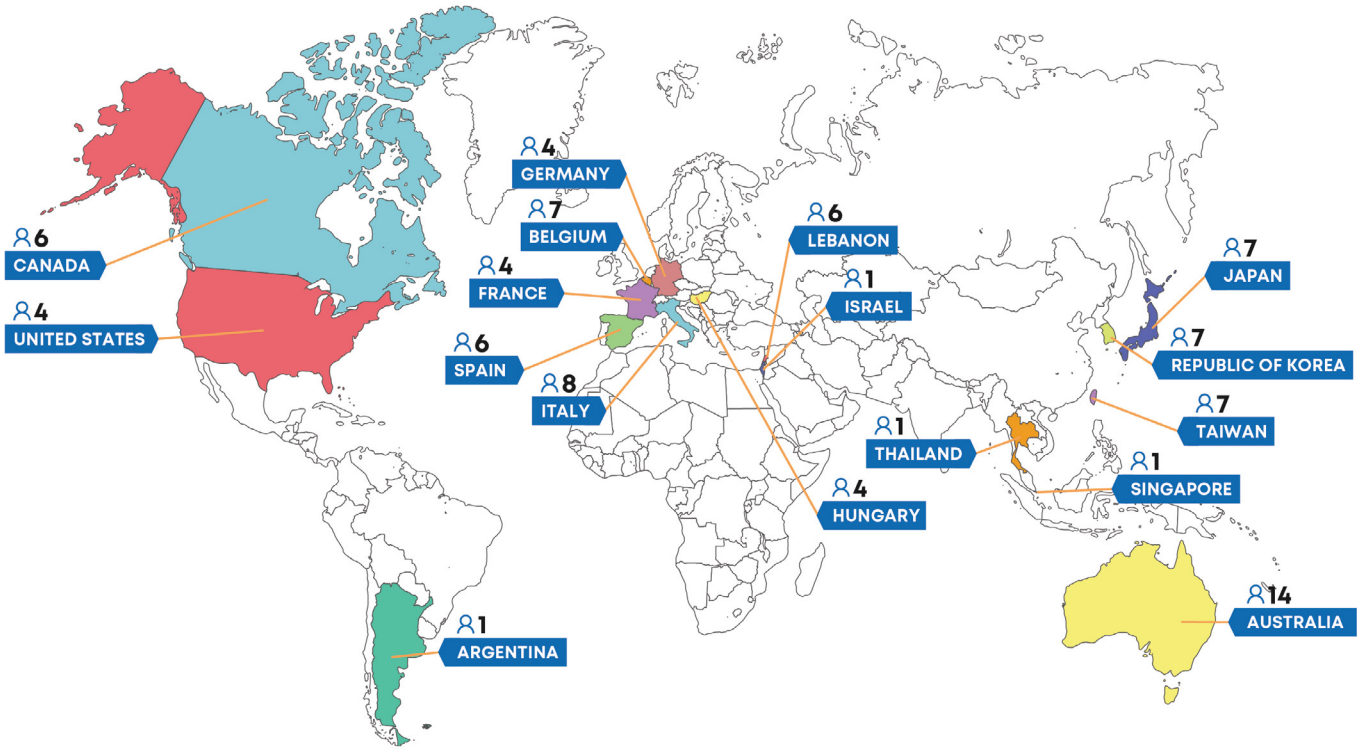
The participants could take part in this trial if they:

1. were 18 years of age or older and had advanced TNBC that was not curable or had spread to other parts of the body (metastatic);
2. had a mass of cancer cells that could be measured;
3. had previously received a specific type of chemotherapy for metastatic cancer;
4. had cancer that had spread and progressed after receiving a previous treatment;
5. had not previously received immune checkpoint inhibitors for cancer treatment.

Participants were randomly assigned to one of three treatment groups. This process is called randomization. It means that each participant could be assigned to any group; it helps to make sure the groups are distributed evenly and fairly.

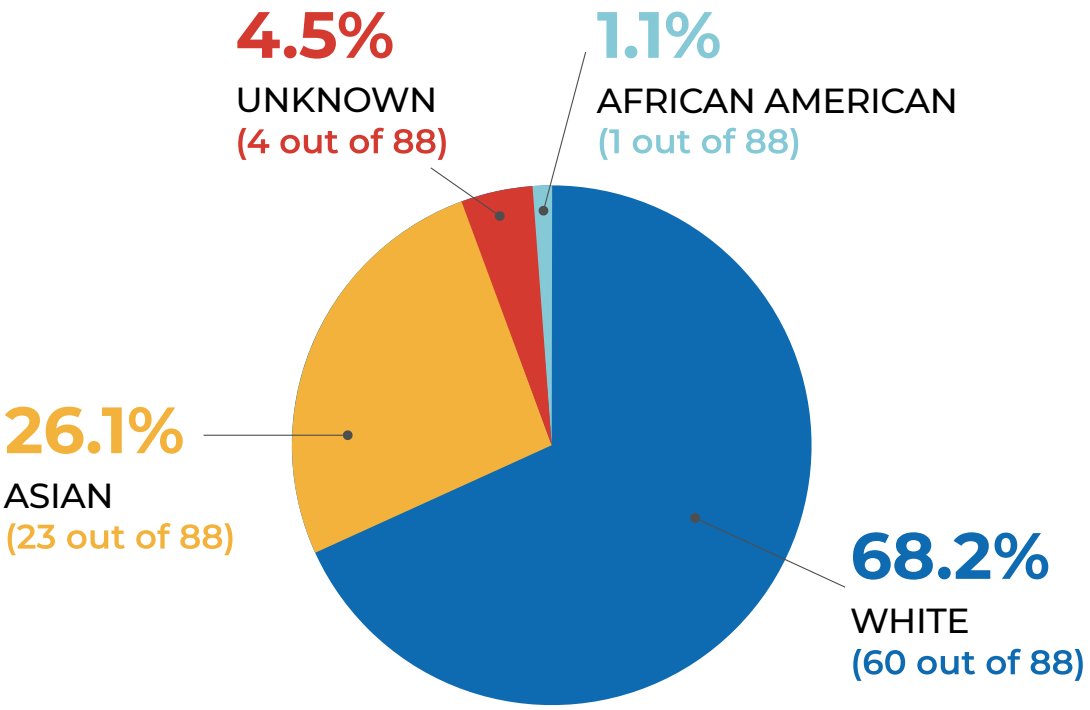
A total of **88 participants from 17 countries** participated in this trial.

Out of those, 20 participants were randomly assigned to receive LAG525 + spartalizumab, 34 participants were assigned to receive LAG525 + spartalizumab + carboplatin, and 34 patients received LAG525 + carboplatin.



The average age of participants in this trial was 53 years. All participants were women (100%). The age of participants ranged from 26 to 71 years.

Participants' Race



What treatments did the participants take?

This was an open-label trial which means that the participants, trial doctors, and trial staff knew what treatment participants were receiving.

TREATMENT DRUGS	
	LAG525, 400 mg + **Spartalizumab,** 300 mg Administered through the vein every 3 weeks
	LAG525, 400 mg + **Spartalizumab,** 300 mg + **Carboplatin,** individualized dose Administered through the vein every 3 weeks
	LAG525, 400 mg + **Carboplatin,** individualized dose Administered through the vein every 3 weeks

What happened during this trial?

SCREENING Up to 3 weeks before treatment

Trial doctors checked participants to make sure they could be in this clinical trial.

Treatment (Open-label)

Participants were randomly assigned to one of the following 3 treatment groups:

Group 1	Group 2	Group 3
LAG525 400 mg every 3 weeks + **Spartalizumab** 300 mg every 3 weeks	**LAG525** 400 mg every 3 weeks + **Spartalizumab** 300 mg every 3 weeks + **Carboplatin** Individualized dose every 3 weeks	**LAG525** 400 mg every 3 weeks + **Carboplatin** Individualized dose every 3 weeks

The doctors checked the effectiveness and afety of the treatment.

Enrollment in Group 1 stopped early because of an increased number of participants who stopped trial treatment due to worsening of their cancer.

End of treatment

Within 7 days of last dose

Follow-Up

Safety

Up to 5 months after the last dose of LAG525/ Spartalizumab
or
start of new cancer treatment
or
up to 1 month after the last dose of carboplatine

Effectiveness

Every 6 weeks during the first 19 months and every 12 weeks thereafter

Survival

Every 12 weeks

What were the main results of this trial?

What was the percentage of participants in each treatment group, whose cancer improved completely or partially after receiving the trial drugs?

Researchers checked the response by measuring the size of specific cancer cell masses regularly, using medical imaging methods such as CT and/or MRI scans up to 6 months after the participants received treatment.

The percentage of participants in whom the cancer cell masses improved completely or partially was higher in Group 2, where the participants received all three drugs, than in Group 1 and Group 3. Also, a total of 5 participants in Group 2 showed complete improvement in the cancer cell masses, while none of the participants in Group 1 and Group 3 had this result.

Overall, these results showed that the trial drugs did not help cancer cell masses disappear or become smaller in most of the participants.

The percentage of participants in each treatment group, whose cancer improved completely or partially after receiving the trial drugs is shown below in the table.

	Group 1 LAG525 + spartalizumab **(20 participants)**	**Group 2** LAG525 + spartalizumab + carboplatin **(34 participants)**	**Group 3** LAG525 + Carboplatin **(34 participants)**
Participants whose cancer improved	1 out of 20 (5%)	11 out of 34 (32.4%)	6 out of 34 (17.6%)

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called “adverse events”.

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug.

An adverse event is an unwanted sign, symptom, or condition that participants have during a trial.
An adverse event is considered “serious” when it is life threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drugs.

When new drugs are being studied, researchers keep track of all of the adverse events that participants have.

This section is a summary of the adverse events that happened during this trial. The websites listed at the end of this summary may have more information about all the adverse events that happened in this trial.

How many participants had adverse events?

In this trial, the majority of participants in Group 1 and all participants in Group 2 and Group 3 experienced at least 1 adverse event.

Note: Only 19 out of 20 participants in Group 1 received treatment since one participant never started the trial drugs.

A total of 3 participants died during the study (on-treatment period) due to complications of their cancer progression considered by the study doctors to be unrelated to the trial treatment. A further 30 participants died during the extended safety follow-up period (five months after the study treatment period ended).

Number of Participants (%) with Adverse Events

	Group 1 LAG525 + spartalizumab **(19 participants)**		**Group 2** LAG525 + spartalizumab + carboplatin **(34 participants)**		**Group 3** LAG525 + Carboplatin **(34 participants)**	
	On -treatment period	Extended safety follow-up period	On -treatment period	Extended safety follow-up period	On -treatment period	Extended safety follow-up period
At least 1 adverse event	17 (89.5%)	0 (0.0%)	34 (100%)	11 (32.4%)	33 (97.1%)	3 (8.8%)
At least 1 serious adverse event	6 (31.6%)	0 (0.0%)	12 (35.3%)	6 (17.7%)	14 (41.2%)	2 (5.9%)
Discontinued (stopped) all study treatment medication due to adverse events	2 (10.5%)	0 (0.0%)	2 (5.9%)	0 (0.0%)	4 (11.8%)	0 (0.0%)
Died	0 (0.0%)	7 (36.8%)	2 (5.9%)	7 (20.6%)	1 (2.9%)	16 (47.1%)

What were the most common serious adverse events?

The most common serious adverse events that happened in at least 5% of the participants in any group are shown below:

Number of Participants (%) With Most Common Serious Adverse Events

	Group 1 LAG525 + spartalizumab (19 participants)		Group 2 LAG525 + spartalizumab + carboplatin (34 participants)		Group 3 LAG525 + Carboplatin (34 participants)	
	On -treatment period	Extended safety follow-up period	On -treatment period	Extended safety follow-up period	On -treatment period	Extended safety follow-up period
Anemia (low levels of red blood cells)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.9%)	1 (2.9%)
Disease progression (worsening og the disease)	1 (5.3%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)
Dyspnoea (difficulty breathing)	1 (5.3%)	0 (0.0%)	2 (5.9%)	0 (0.0%)	3 (8.8%)	0 (0.0%)
Fanconi Syndrome (a disorder of the kidney tubes in which certain substances normally absorbed into the bloodstream are released into the urine instead)	1 (5.3%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)
Hypercalcemia (high blood calcium levels)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Platelet count decreased (low number of components that help blood clot)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pleural effusion (fluid around the lungs)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	2 (5.9%)	0 (0.0%)
Pneumocystis jirovecii pneumonia (a serious lung infection caused by a fungus)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pneumonia (infection of the lungs)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Renal tubular acidosis (high levels of acid in the blood due to kidney damage)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Septic shock (a dangerous drop in blood pressure caused by severe infection)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Subcutaneous abscess (a swollen area under the skin where pus has collected)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 20% of the participants in any group are shown below:

Number of Participants (%) With Most Common Non-Serious Adverse Events

	Group 1 LAG525 + spartalizumab (19 participants)		Group 2 LAG525 + spartalizumab + carboplatin (34 participants)		Group 3 LAG525 + Carboplatin (34 participants)	
	On -treatment period	Extended safety follow-up period	On -treatment period	Extended safety follow-up period	On -treatment period	Extended safety follow-up period
Anemia (low levels of red blood cells)	1 (5.3%)	0 (0.0%)	20 (58.8%)	5 (14.7%)	19 (55.9%)	1 (2.9%)
Nausea	3 (15.8%)	0 (0.0%)	18 (52.9%)	2 (5.9%)	13 (38.2%)	1 (2.9%)
Platelet count decreased (low number of components that help blood clot)	1 (5.3%)	0 (0.0%)	14 (41.2%)	2 (5.9%)	9 (26.5%)	0 (0.0%)
Fatigue (tiredness)	2 (10.5%)	0 (0.0%)	11 (32.4%)	1 (2.9%)	12 (35.3%)	0 (0.0%)
Asthenia (weakness)	0 (0.0%)	0 (0.0%)	11 (32.4%)	0 (0.0%)	5 (14.7%)	0 (0.0%)
Neutrophil count decreased (low numbers of neutrophils, a type of white blood cell that fights infection)	0 (0.0%)	0 (0.0%)	11 (32.4%)	2 (5.9%)	6 (17.7%)	0 (0.0%)
Back pain	1 (5.3%)	0 (0.0%)	7 (20.6%)	2 (5.9%)	3 (8.8%)	0 (0.0%)
Constipation	3 (15.8%)	0 (0.0%)	7 (20.6%)	1 (2.9%)	16 (47.1%)	0 (0.0%)
Vomiting	0 (0.0%)	0 (0.0%)	7 (20.6%)	1 (2.9%)	7 (20.6%)	0 (0.0%)
Diarrhea	0 (0.0%)	0 (0.0%)	5 (14.7%)	2 (5.9%)	7 (20.6%)	0 (0.0%)
Headache	2 (10.5%)	0 (0.0%)	8 (23.5%)	0 (0.0%)	4 (11.8%)	1 (2.9%)
Cough	2 (10.5%)	0 (0.0%)	7 (20.6%)	0 (0.0%)	4 (11.8%)	0 (0.0%)

How was this trial useful?

This trial helped researchers learn about the effectiveness and safety of LAG525 when administered in three different combinations with spartalizumab and carboplatin, in patients with advanced triple-negative breast cancer.

The results from this trial showed that LAG525 did not help to significantly shrink or reduce cancer cell masses in any of the treatment groups

Therefore, LAG525 was not considered to be effective for the treatment of TNBC, and the researchers are not planning to continue developing this drug for the treatment of breast cancer.

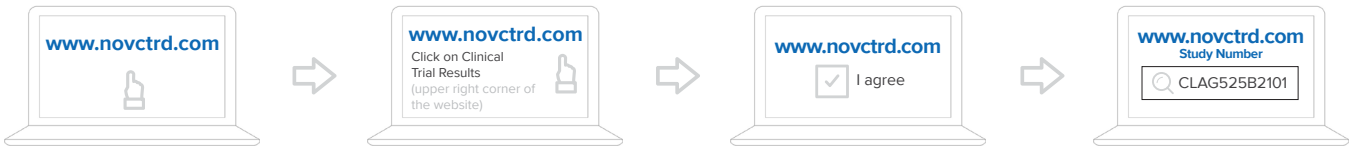
The safety information for all three treatment combinations was consistent with what is known about these drugs when used individually or in combination.

If there are any questions about these trial results, please talk to the doctor or staff at your trial site.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).

Please follow the below steps:



You can find more information about this trial on the following websites:

1. www.clinicaltrials.gov Use the NCT identifier NCT03499899 in the search field.
2. https://www.clinicaltrialsregister.eu/ctr-search Use the EudraCT identifier Eudra 2017-004865-28 in the search field.

Full clinical trial title: A phase II open-label, randomized, three-arm, multicenter study of LAG525 given in combination with spartalizumab (PDR001), or with spartalizumab and carboplatin, or with carboplatin, as first or second-line therapy in patients with advanced triple-negative breast cancer.

Thank You!

Thank you to all trial participants. Clinical trial 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 test new medical treatments for patients.

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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