Clinical Study Results

MedImmune
A member of the AstraZeneca Group

Research Sponsor: MedImmune, Ltd.

Drug Studied: MEDI4276

Study Title: A study to learn about the safety of MEDI4276 in people with HER2 solid tumors

Thank you!

Thank you to the participants who took part in the clinical study for the study drug MEDI4276. You and all the participants helped researchers learn more about using MEDI4276 to help people with advanced breast or stomach cancer.

MedImmune sponsored this study and thinks it is important to share the results. An independent, non-profit organization called CISCRP helped prepare this summary of the study results for you. We hope it helps you understand and feel proud of your important role in medical research.

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

What is happening with the study now?

The participants were in the study for up to about 42 weeks. But, the entire study took about 2.5 years to finish. The study started in September 2015 and ended in May 2018. The study included 47 participants in the United States.

The researchers planned to include up to 216 participants in this study. But, the researchers ended the study early because MEDI4276 was not shrinking the participants' tumors enough, the participants had medical problems, and the results of the study were not as expected.

The sponsor reviewed the data collected when the study ended and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers are looking for a better way to treat people with advanced breast or stomach cancers who have a protein called “human epidermal growth factor receptor 2” on their tumor. This protein is also called HER2 receptor.

HER2 is found on the surface of a cancer cell and causes the cancer to grow quickly. There are some treatments for this type of cancer, but they do not help all patients.

MEDI4276 is thought to attach to the HER2 receptor, causing the cells in the tumor to die.

Before a drug can be approved for patients to take, researchers do clinical studies to find out how safe it is and how it works. In this study, the researchers wanted to learn more about the safety of MEDI4276 and if it worked in participants with the HER2 receptor.

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

- Did MEDI4276 affect the participants’ overall health?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of men and women with breast or stomach cancer who had a HER2 receptor. The participants were 39 to 76 years old when they joined. All the participants had advanced breast or stomach cancer that could not be surgically removed.

What kind of study was this?

This was an “open-label” study. This means the researchers and the participant knew what the participant was taking. All of the participants in this study got MEDI4276 through a needle into their vein, also called intravenous infusion. The researchers wanted to learn how different doses of MEDI4276 affected the participants. They originally planned that the study would have 2 parts. But, the researchers ended the study early because MEDI4276 was not shrinking the participants’ tumors and the results of the first part were not as expected.

There were 9 different groups of participants in this study. The dose of MEDI4276 was different in each group. It was measured in milligrams per kilogram of body weight, also known as mg/kg. The study doctors studied how the dose affected the participants in each group, before giving MEDI4276 to the next group of participants.

The chart below shows the treatments the participants got.

Treatment group	Number of participants	Dose of MEDI4276
Group 1	3	0.05 mg/kg
Group 2	3	0.1 mg/kg
Group 3	3	0.2 mg/kg
Group 4	3	0.3 mg/kg
Group 5	6	0.4 mg/kg
Group 6	3	0.5 mg/kg
Group 7	11	0.6 mg/kg
Group 8	12	0.75 mg/kg
Group 9	3	0.9 mg/kg

What happened during the study?

Before giving the participants any MEDI4276, the study doctors did a physical exam and checked to make sure the participants could join the study. The study doctors:

- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG
- took pictures of the heart using an echocardiogram or a multigated acquisition, also called MUGA, scan

If needed, the study doctors also took pictures of the liver using magnetic resonance cholangiopancreatography, also called MRCP.

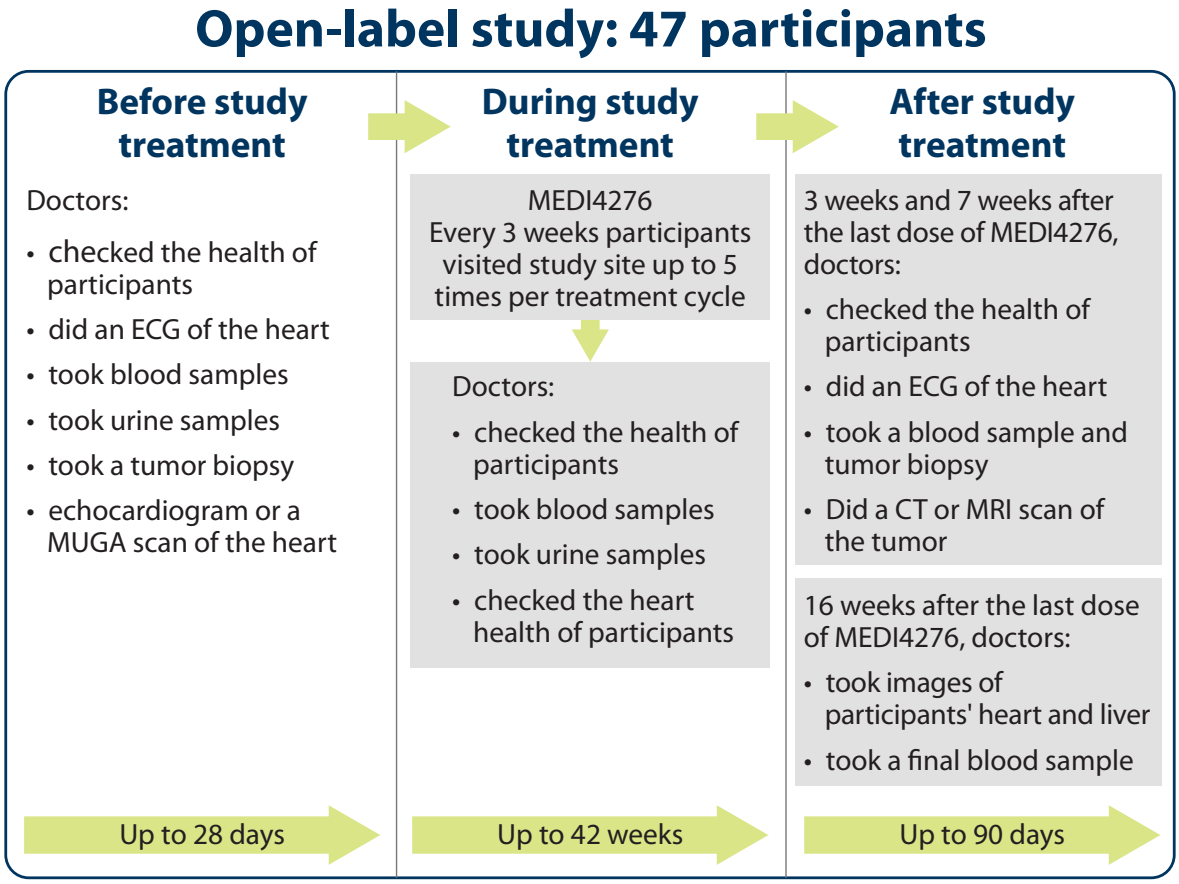
Some participants may have had a tumor biopsy. In this procedure, the doctor uses a needle to take some of the tumor tissue to examine.

During the study, the participants got MEDI4276 infusions every 3 weeks. They visited their study site up to 5 times per treatment cycle. At some of these visits, the study doctors:

- did a physical exam
- took blood samples
- took urine samples
- measured the participants' vital signs
- checked the participants' heart health using an ECG

3 weeks after the last dose of MEDI4276, the study doctors did a physical exam, took the participants' weight, recorded any changes in disease, took a blood sample, recorded vital signs, checked the participants' heart health using an ECG, and took pictures of the heart using an echocardiogram. They repeated these assessments 7 weeks after the last dose of MEDI4276. About 16 weeks after the last dose of MEDI4276, the study doctors took images of the participants' heart and took a final blood sample.

The figure below summarizes the study process.



What were the results of the study?

This is a summary of the main results from this study. The individual results each participant had might be different and are not presented in this summary.

Researchers look at the results of many studies to decide which treatments work best and are safest. Other studies may provide new information or different results. Always talk to a doctor before making any treatment change.

The websites listed at the end of this summary may have a full report of the study results.

Did MEDI4276 affect the participants' overall health?

To answer this question, the researchers compared the results of the tests and measurements that the study doctors took before, during, and after the study. The researchers also collected information about how many "adverse events" the participants had. An adverse event is any medical problem that happens during the study. Adverse events are considered "serious" when they are life-threatening, cause lasting problems, or require hospital care. Adverse events may or may not be caused by the study drug.

The study doctors also counted the number of dose-limiting toxicities the participants had during the study. A dose-limiting toxicity is a medical problem that is severe enough to stop the study doctor from increasing the participant's dose of study treatment. A dose-limiting toxicity is also known as a DLT.

In Group 5, 16.7% of participants had a dose-limiting toxicity reaction. This was 1 out of 6 participants who received the 0.4 mg/kg dose of MEDI4276.

In Group 7, 9.1% of participants had a dose-limiting toxicity reaction. This was 1 out of 11 participants who received the 0.6 mg/kg dose of MEDI4276.

In Group 9, 66.7% of participants had a dose-limiting toxicity reaction. This was 2 out of 3 participants who received the 0.9 mg/kg dose of MEDI4276.

Overall, the researchers found that the health of the participants during the study was the same in each group. There were small differences in the safety results of each group. But, the differences were too small for the researchers to know if MEDI4276 affected these results.

How many participants had adverse events?

There were 97.9% of participants who had at least 1 adverse event during the study. This was 46 out of 47 participants.

There were 29.8% of participants with at least 1 serious adverse event during the study. This was 14 out of 47 participants.

There were 10.6% of participants who withdrew from the study due to adverse events. This was 5 out of 47 participants. These were all thought to be related to the study drug.

How many participants had serious adverse events?

There were 29.8% of participants with at least 1 serious adverse event during the study. This was 14 out of 47 participants. More detail can be found in the tables below.

Serious adverse event	Group 1 (Out of 3 participants)	Group 2 (Out of 3 participants)	Group 3 (Out of 3 participants)	Group 4 (Out of 3 participants)	Group 5 (Out of 6 participants)
Dehydration due to loss of body fluids	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
Stomach pain	0.0% (0)	33.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Diarrhea	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
High levels of bilirubin in the blood which indicates liver damage	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
Nausea	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Small intestine blockage	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Vomiting	0.0% (0)	33.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)
High levels of a liver enzyme (ALT)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
Thickened blood	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
High level of a liver enzyme (AST)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
High levels of a liver enzyme (ALP)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
Bacteria present in the blood	0.0% (0)	33.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Skin infection	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Language impairment	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Mental state changes	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Cough	0.0% (0)	0.0% (0)	33.3% (1)	0.0% (0)	0.0% (0)

Serious adverse event	Group 6 (Out of 3 participants)	Group 7 (Out of 11 participants)	Group 8 (Out of 12 participants)	Group 9 (Out of 3 participants)	Total (Out of 47 participants)
Dehydration due to loss of body fluids	0.0% (0)	9.1% (1)	8.3% (1)	0.0% (0)	6.4% (3)
Stomach pain	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	4.3% (2)
Diarrhea	0.0% (0)	9.1% (1)	0.0% (0)	33.3% (1)	4.3% (2)
High levels of bilirubin in the blood which indicates liver damage	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	4.3% (2)
Nausea	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	2.1% (1)
Small intestine blockage	0.0% (0)	0.0% (0)	8.3% (1)	0.0% (0)	2.1% (1)
Vomiting	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	2.1% (1)
High levels of a liver enzyme (ALT)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	2.1% (1)
Thickened blood	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	2.1% (1)
High level of a liver enzyme (AST)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	2.1% (1)
High levels of a liver enzyme (ALP)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	2.1% (1)
Bacteria present in the blood	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	2.1% (1)
Skin infection	0.0% (0)	9.1% (1)	0.0% (0)	0.0% (0)	2.1% (1)
Language impairment	0.0% (0)	9.1% (1)	0.0% (0)	0.0% (0)	2.1% (1)
Mental state changes	0.0% (0)	9.1% (1)	0.0% (0)	0.0% (0)	2.1% (1)
Cough	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	2.1% (1)

23 participants died during the study. None of these deaths were related to adverse events. The deaths were related to the advanced stomach cancer or advanced breast cancer the participants had.

What adverse events did the participants have?

The most common adverse event during the study was nausea.

Adverse events that occurred in 10% or more of the total study participants are listed in the tables below. This is 5 out of 47 participants.

Adverse event	Group 1 (Out of 3 participants)	Group 2 (Out of 3 participants)	Group 3 (Out of 3 participants)	Group 4 (Out of 3 participants)	Group 5 (Out of 6 participants)
Nausea	33.3% (1)	66.7% (2)	33.3% (1)	100.0% (3)	83.3% (5)
Fatigue	0.0% (0)	100.0% (3)	66.7% (2)	33.3% (1)	50.0% (3)
Vomiting	33.3% (1)	66.7% (2)	0.0% (0)	0.0% (0)	66.7% (4)
Diarrhea	33.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (2)
High levels of a liver enzyme (AST)	33.3% (1)	0.0% (0)	33.3% (1)	33.3% (1)	33.3% (2)
High levels of a liver enzyme (ALT)	33.3% (1)	0.0% (0)	33.3% (1)	33.3% (1)	16.7% (1)
Lower appetite	0.0% (0)	33.3% (1)	0.0% (0)	0.0% (0)	33.3% (2)
Partial or complete absence of hair	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Weight loss	33.3% (1)	33.3% (1)	33.3% (1)	0.0% (0)	16.7% (1)
Constipation	0.0% (0)	0.0% (0)	66.7% (2)	0.0% (0)	0.0% (0)
Abdominal pain	0.0% (0)	33.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)
High levels of a liver enzyme (ALP)	0.0% (0)	0.0% (0)	33.3% (1)	0.0% (0)	16.7% (1)
Dehydration	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	16.7% (1)
Difficulty with breathing	0.0% (0)	0.0% (0)	33.3% (1)	0.0% (0)	0.0% (0)
Urinary tract infection	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
Low potassium	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)

Adverse event	Group 6 (Out of 3 participants)	Group 7 (Out of 11 participants)	Group 8 (Out of 12 participants)	Group 9 (Out of 3 participants)	Total (Out of 47 participants)
Nausea	100.0% (3)	45.5% (5)	83.3% (10)	100.0% (3)	70.2% (33)
Fatigue	33.3% (1)	36.4% (4)	75.0% (9)	100.0% (3)	55.3% (26)
Vomiting	66.7% (2)	54.5% (6)	41.7% (5)	66.7% (2)	46.8% (22)
Diarrhea	33.3% (1)	45.5% (5)	66.7% (8)	100.0% (3)	42.6% (20)
High levels of a liver enzyme (AST)	0.0% (0)	45.5% (5)	66.7% (8)	66.7% (2)	42.6% (20)
High levels of a liver enzyme (ALT)	0.0% (0)	45.5% (5)	66.7% (8)	66.7% (2)	40.4% (19)
Lower appetite	33.3% (1)	36.4% (4)	75.0% (9)	33.3% (1)	38.3% (18)
Partial or complete absence of hair	0.0% (0)	36.4% (4)	50.0% (6)	66.7% (2)	25.5% (12)
Weight loss	66.7% (2)	9.1% (1)	25.0% (3)	66.7% (2)	25.5% (12)
Constipation	100.0% (3)	36.4% (4)	16.7% (2)	33.3% (1)	25.5% (12)
Abdominal pain	33.1% (1)	9.1% (1)	50.0% (6)	33.3% (1)	21.3% (10)
High levels of a liver enzyme (ALP)	33.3% (1)	36.4% (4)	8.3% (1)	66.7% (2)	21.3% (10)
Dehydration	0.0% (0)	27.3% (3)	25.0% (3)	66.7% (2)	21.3% (10)
Difficulty with breathing	0.0% (0)	9.1% (1)	33.3% (4)	66.7% (2)	17.0% (8)
Urinary tract infection	0.0% (0)	18.2% (2)	33.3% (4)	33.3% (1)	17.0% (8)
Low potassium	0.0% (0)	9.1% (1)	33.3% (4)	100.0% (3)	17.0% (8)

What medical problems did the participants have during the study?

This section is a summary of the adverse events the participants had during the study that the study doctors thought might be related to the study drug. These are called “adverse reactions”. An adverse reaction is considered “serious” when it is life-threatening, cause lasting problems, or requires hospital care.

These adverse reactions may or may not be caused by the study drug. A lot of research is needed to know whether a drug causes an adverse reaction.

The website(s) listed at the end of this summary may have other information about adverse reactions or other medical problems that happened during this study.

How many participants had serious adverse reactions?

There were 8.5% of participants who had at least 1 serious adverse reaction. This was 4 out of 47 participants.

None of the participants died due to serious adverse reactions during this study.

The tables below show the serious adverse reactions that happened during this study.

Serious adverse reaction	Group 1 (Out of 3 participants)	Group 2 (Out of 3 participants)	Group 3 (Out of 3 participants)	Group 4 (Out of 3 participants)	Group 5 (Out of 6 participants)
High levels of a protein in the blood (bilirubin)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
High levels of a liver enzyme (ALT)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
High levels of a liver enzyme (AST)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
High levels of a liver enzyme (ALP)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
Dehydration	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Nausea	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Diarrhea	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)

Serious adverse reaction	Group 6 (Out of 3 participants)	Group 7 (Out of 11 participants)	Group 8 (Out of 12 participants)	Group 9 (Out of 3 participants)	Total (Out of 47 participants)
High levels of a protein in the blood (bilirubin)	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	4.3% (2)
High levels of a liver enzyme (ALT)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	2.1% (1)
High levels of a liver enzyme (AST)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	2.1% (1)
High levels of a liver enzyme (ALP)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Dehydration	0.0% (0)	0.0% (0)	8.3% (1)	0.0% (0)	2.1% (1)
Nausea	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	2.1% (1)
Diarrhea	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	2.1% (1)

How many participants had adverse reactions?

There were 91.5% of participants who had at least 1 adverse reaction that the study doctors thought might be related to the study drug during the study. This was 43 out of 47 participants.

There were 10.6% of participants who left the study because of adverse reactions. This was 5 out of 47 participants.

What adverse reactions did the participants have?

The most common adverse reaction during the study was nausea.

The tables on the next page show the most common adverse reactions that happened in more than 20% of the participants during the study. There were other adverse reactions, but these happened in fewer participants.

Adverse reaction	Group 1 (Out of 3 participants)	Group 2 (Out of 3 participants)	Group 3 (Out of 3 participants)	Group 4 (Out of 3 participants)	Group 5 (Out of 6 participants)
Nausea	33.3% (1)	66.7% (2)	33.3% (1)	100% (3)	66.7% (4)
Fatigue	0.0% (0)	66.7% (2)	33.3% (1)	33.3% (1)	33.3% (2)
High levels of a liver enzyme (AST)	33.3% (1)	0.0% (0)	33.3% (1)	33.3% (1)	33.3% (2)
High levels of a liver enzyme (ALT)	33.3% (1)	0.0% (0)	33.3% (1)	33.3% (1)	16.7% (1)
Vomiting	33.3% (1)	33.3% (1)	0.0% (0)	0.0% (0)	66.7% (4)
Diarrhea	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
Decreased appetite	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)
High levels of a protein in the blood (ALP)	0.0% (0)	0.0% (0)	33.3% (1)	0.0% (0)	16.7% (1)

Adverse reaction	Group 6 (Out of 3 participants)	Group 7 (Out of 11 participants)	Group 8 (Out of 12 participants)	Group 9 (Out of 3 participants)	Total (Out of 47 participants)
Nausea	100% (3)	27.3% (3)	66.7% (8)	100% (3)	59.6% (28)
Fatigue	33.3% (1)	18.2% (2)	75.0% (9)	100% (3)	44.7% (21)
High levels of a liver enzyme (AST)	0.0% (0)	45.5% (5)	66.7% (8)	66.7% (2)	42.6% (20)
High levels of a liver enzyme (ALT)	0.0% (0)	45.5% (5)	66.7% (8)	66.7% (2)	40.4% (19)
Vomiting	66.7% (2)	27.3% (3)	41.7% (5)	66.7% (2)	38.3% (18)
Diarrhea	0.0% (0)	27.3% (3)	58.3% (7)	100% (3)	29.8% (14)
Decreased appetite	0.0% (0)	36.4% (4)	66.7% (8)	33.3% (1)	29.8% (14)
High levels of a protein in the blood (ALP)	33.3% (1)	36.4% (4)	8.3% (1)	66.7% (2)	21.3% (10)

How has this study helped patients and researchers?

This study helped researchers learn about the safety of MEDI4276 in participants with breast or stomach cancer who had a HER2 receptor.

Researchers look at the results of many studies to decide which treatments work best and are safest. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Further clinical studies with MEDI4276 are not planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If a full report of the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02576548"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5760C00001"** into the search box, and click **"Find a Study"**.

Full study title: A Phase 1/ 2 Multicenter, Open-label, Dose-escalation, and Dose-expansion Study to Evaluate the Safety, Pharmacokinetics, Immunogenicity, and Antitumor Activity of MEDI4276 in Subjects with Select HER2 expressing Advanced Solid Tumors

National Clinical Trials number: NCT02576548

AstraZeneca Protocol Number: D5760C00001

MedImmune Ltd., an AstraZeneca company, sponsored this study and has its headquarters in Mölndal, Sweden.

The phone number for the AstraZeneca Information Center is +1 877 240 9479.

Thank you!

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

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting patients for clinical studies, nor is it involved in conducting clinical studies.

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