Clinical Trial RESULTS

Research Sponsor:	F. Hoffmann-La Roche, Ltd. and Genentech, Inc.
Drug Studied:	Trastuzumab emtansine (T-DM1)
National Clinical Trial #:	NCT01196052
Protocol #:	BO22857/TDM4874g
Study Date:	October 2010 to June 2013

Thank you!

As a clinical study participant, you belong to a large community of participants around the world. You help researchers answer important health questions and discover new medical treatments.

Thank you for taking part in the clinical study for the study drug T-DM1. Your study began in October 2010 and finished in June 2013. Also known as trastuzumab emtansine, T-DM1 was studied for use in patients with breast cancer after chemotherapy. You and 152 other patients helped researchers find out how safe T-DM1 is for people with early-stage HER2-positive breast cancer.

F. Hoffmann-La Roche and Genentech, the sponsors of this study, think it is important for you to know the results. The sponsors asked an independent non-profit organization called CISCRP to prepare this summary of the results for you. We hope it helps you understand and feel proud of your key role in medical research. If you have questions about the results, please speak with the doctor, research nurse, or other team member at your study site.

WHAT'S HAPPENED SINCE MY STUDY ENDED?

The entire study took almost three years to finish, and included patients from eight countries around the world. The sponsor presented early results from this study at International Scientific Congress in May 2012, and final results will be presented at San Antonio Breast Cancer Symposium in December 2013. A total of 148 patients received at least 1 dose of T-DM1. This is a summary of results from those patients.

WHY WAS THE RESEARCH NEEDED?

Researchers were looking for a better way to treat HER2-positive breast cancers, using a biological treatment that directly attacks cancer cells.

When breast cancer is called HER2-positive, it means that the surfaces of the cancer cells have a large amount of a protein called human epidermal growth factor receptor 2 (HER2). A large amount of the HER2 protein can cause cancer cells to grow, multiply and spread. From other clinical studies, researchers knew that an antibody called trastuzumab (Herceptin®) blocks the HER2 protein. Trastuzumab is approved by regulatory authorities as a treatment for HER2-positive breast cancer. However, treatment with trastuzumab can cause heart problems.

In your study, patients received the study drug T-DM1. T-DM1 is composed of a chemotherapy drug (DM1) linked to Herceptin® (trastuzumab) that attaches to HER2 on cells. From clinical studies, researchers know that T-DM1 is active against HER2-positive, metastatic breast cancer (cancer that has spread). Use of T-DM1 should be limited to patients who were previously treated with trastuzumab and a class of chemotherapy drugs for metastatic disease called "taxanes".

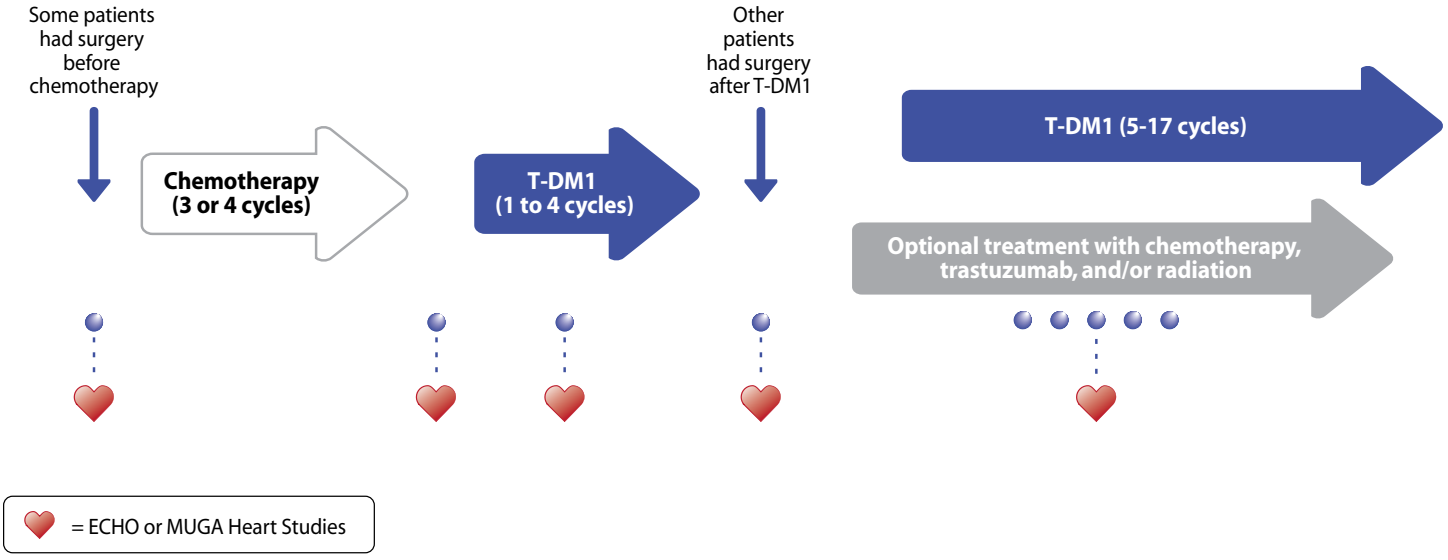
Now researchers wanted to know how safe T-DM1 is after chemotherapy for patients with early-stage, HER2-positive breast cancer. The results of your study helped answer three important questions:

- What percentage of patients treated with T-DM1 developed severe heart damage?
- Does T-DM1 affect the heart in other ways?
- Do patients have harmful effects not involving the heart?

All of the patients in your study were at least 18 years old and had early-stage, HER2-positive breast cancer. All patients were healthy enough to carry out their usual activities and were going to be treated with chemotherapy.

WHAT HAPPENED DURING THE STUDY?

Patients received different types of cancer treatment at different times. This was based on what their doctor thought best. As shown in the diagram below, some patients started with surgery, then had chemotherapy, and then T-DM1. Other patients started with chemotherapy, then received T-DM1, and then had surgery afterward.



Patients then had additional treatment with T-DM1, and in some cases chemotherapy, radiation and/or trastuzumab. In total, patients could have up to 17 cycles of T-DM1. In each cycle, T-DM1 was infused into a vein once every three weeks.

During this study, researchers regularly checked the health of patients' hearts. They used heart studies including echocardiogram (ECHO) and multigated acquisition (MUGA) scan. These tests were done before and after chemotherapy. They were also done after cycles 2 and 4 of T-DM1, every 4 cycles of T-DM1 after that, and before and after each optional new treatment. The final tests were done 3 and 6 months after treatment. If ECHO or MUGA showed medically significant decreases in heart function during the study, patients stopped treatment with T-DM1.

Researchers also kept track of all medical problems that patients had. These are known as "adverse events", which may or may not be caused by the study drug.

WHAT WERE THE STUDY RESULTS?

Below is a summary of the medical questions that were asked in this study, and the study results.

What percentage of patients had severe heart damage?

0%
OF PATIENTS HAD SEVERE HEART DAMAGE

Of the 148 patients in this study who received T-DM1, none had severe heart damage.

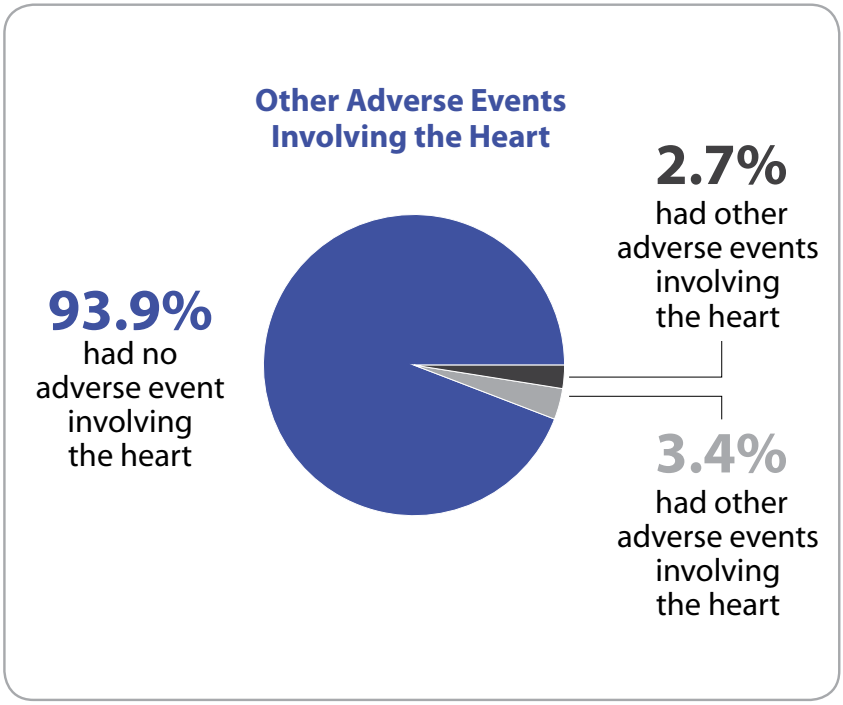
Heart damage would have been considered "severe" if patients died from heart disease, or had moderate to severe congestive heart failure (CHF). CHF is caused by weakness of the heart muscle. Patients with moderate CHF have shortness of breath and reduced heart function after minimal activity. Patients with severe CHF have these symptoms even when resting.

The measure of heart function in this study was "left ventricular ejection fraction" (LVEF). This measure remained about the same for patients throughout the study, which suggests that T-DM1 did not affect the heart muscle.

Were there other adverse events involving the heart?

Yes. Five patients (3.4%) had other T-DM1 related adverse events involving the heart, and 4 patients (2.7%) experienced decline in LVEF (worsening heart function) that did not cause symptoms.

The table below summarizes the adverse events involving the heart that patients in this study had.



Adverse Events Involving the Heart (Out of 148 Patients)	
Moderate to severe CHF or death from heart disease	0 patients (0%)
Decreased LVEF* causing symptoms	0 patients (0%)
Decreased LVEF* related to T-DM1, but not causing symptoms	4 patients (2.7%)
Patients who stopped T-DM1 because of adverse events involving the heart	1 patients (0.7%)
Adverse events involving the heart related to T-DM1	5 patients (3.4%)

* LVEF (Left Ventricular Ejection Fraction) is a measure of how well patients' hearts were pumping.

One patient had a severe heart beat rhythm problem and palpitations. One patient had a mild to moderate failure in one of the heart valves, allowing some blood to flow in the wrong direction. Three other patients had palpitations, sensations of heart pounding or fluttering.

How safe and effective is T-DM1 after chemotherapy for women with early-stage, HER2-positive breast cancer?

Researchers are still working to find this out. Although this study was not designed to test how well T-DM1 works, doctors evaluated the tissue removed at surgery for evidence of cancer in the breast or lymph nodes. Out of the 50 patients who had surgery after chemotherapy and 4 cycles of T-DM1, 22 patients (44%) still had microscopic evidence of cancer in the removed tissue, and 28 patients (56%) did not.

More research is needed to understand these results. Researchers and doctors look at findings from many studies to understand which treatments work best and are safest for patients.

WHAT OTHER ADVERSE EVENTS DID PATIENTS HAVE?

The main purpose of this study was to see if patients receiving T-DM1 had side effects involving the heart. However, the researchers kept track of all medical problems that patients had. These medical problems are called "adverse events", and may or may not be caused by the study drugs. A list of adverse events is an important part of the study results. This section tells you about the adverse events found in your study.

What serious adverse events did patients have?

An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care. Fifteen patients (10.1%) had serious adverse events during T-DM1 therapy, though they may not all have been related to T-DM1. No patients died in this study.

What were the most common adverse events during T-DM1 therapy?

The most common adverse events were nausea, headache, nose bleeds, weakness, fever, and fatigue. The table below shows how many patients had these adverse events.

Most Common Adverse Events in Patients Receiving T-DM1 (Out of 148 Patients)	
Nausea	56 patients (37.8%)
Headache	55 patients (37.2%)
Nose bleeds	47 patients (31.8%)
Weakness	45 patients (30.4%)
Fever	39 patients (26.4%)
Fatigue	34 patients (23.0%)
Joint pain	33 patients (22.3%)
Low platelet count	32 patients (21.6%)
Muscle pain	31 patients (20.9%)
Vomiting	25 patients (16.9%)
Rash	24 patients (16.2%)

How many patients stopped receiving T-DM1 because of adverse events?

In total, 20 out of 148 patients (13.5%) stopped receiving T-DM1 because of adverse events.

WHERE CAN I LEARN MORE ABOUT THIS STUDY?

This summary of the clinical study results is available online at *www.ciscrp.org/NCT01196052*. At that webpage, you will find a link to the full scientific presentation. If you have questions about the results, please speak with the doctor, research nurse, or other team member at your study site.

Thank you

It is said that the greatest gift is one which is given anonymously, giving when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge and benefits public health. Thank you for the gift of your participation in clinical research.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

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 trials, nor is it involved in conducting clinical trials.