Clinical Trial Summary

Bristol-Myers Squibb

A trial to compare how 2 different doses of ipilimumab acted in people with advanced melanoma tumors

Drug Studied: Ipilimumab
Trial Sponsor: Bristol-Myers Squibb
Trial Start: February 2012
Trial End: August 2017

Thank you

Thank you for taking part in the Checkmate 742 clinical trial for ipilimumab. You and all of the patients helped the researchers learn more about using ipilimumab to treat patients with advanced melanoma tumors.

Bristol-Myers Squibb sponsored this trial and thinks it is important to share the results with you and the public. Bristol-Myers Squibb reviewed the results of the trial when it ended. An independent, non-profit organization called CISCRP and a medical writing organization called Synchrogenix helped prepare this summary of the trial results for you.

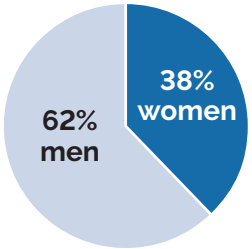
We hope this information allows you, and all patients, to understand the important role you are playing in the advancement of medical science. If you have questions about the results, please speak with a doctor or staff at your trial site.

Who took part in this trial?

The trial had 2 parts. If the patients' tumors stayed the same or got smaller after Part 1, the patients continued into Part 2.

Each patient was in the trial for up to about 5 years. The trial started in February 2012 and ended in August 2017.

727 patients



21 countries

Argentina	France	Norway
Australia	Germany	Poland
Austria	Hungary	South Africa
Belgium	Israel	Spain
Canada	Italy	Sweden
Czech Republic	Mexico	United Kingdom
Denmark	Netherlands	United States

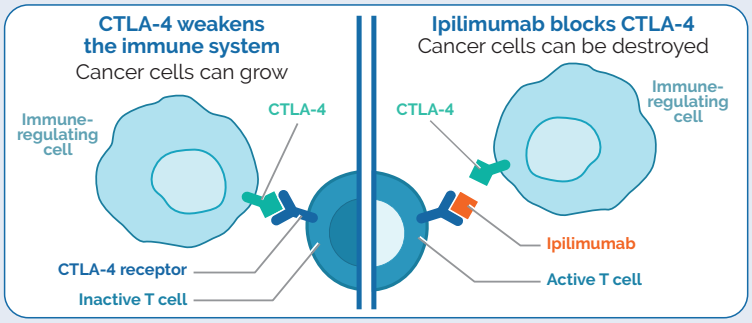
Why was the research needed?

Researchers are looking for a better way to treat advanced melanoma, which is a type of skin cancer. Before a treatment is available to all patients, researchers study it in trials to learn how it works and how safe it is.

The researchers in the trial wanted to compare 2 different doses of ipilimumab to see how each dose acted in people with advanced melanoma. They also wanted to find out if the patients had any medical problems during the trial.

Many cancers, including melanoma, can weaken your immune system. When the immune system does not work properly, the cancer can grow and spread.

Certain cells in the immune system can destroy cancer cells. But a protein in the body called CTLA-4 can make the immune system not work properly. When this happens, your immune system cannot destroy cancer cells. Blocking CTLA-4 allows your immune system to destroy cancer cells.



The trial drug, ipilimumab, is a type of antibody that can block CTLA-4. Antibodies are normally made by the body's T cells to fight off infection. But researchers are now able to use antibodies as medicines to treat a variety of conditions, including advanced melanoma. Researchers hope that by blocking CTLA-4, your immune system will keep working and help destroy cancer cells.

Ipilimumab is already used to treat advanced melanoma tumors. But, researchers wanted to study a new dose of ipilimumab and compare with the two doses.

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

- Did the patients who got the trial dose of ipilimumab live longer than the patients who got the approved dose?
- Did ipilimumab affect the patients in other ways?
- Did ipilimumab affect quality of life?
- What medical problems did the patients have?

To answer these questions, the researchers asked for the help of men and women with advanced melanoma tumors. Everyone in the trial was between 19 and 89 years of age when they joined.

What treatments did the patients take?

This was a "double-blind" trial. This means none of the patients, doctors, or other trial staff knew what treatment each patient got. Some trials are done this way because knowing what treatment the patients are getting can affect the results of the trial.

When the trial ended, Bristol-Myers Squibb found out which treatment each patient got. This allowed researchers to create a report of the results.

All of the patients in the trial got ipilimumab through a needle put into their vein. This is called an intravenous infusion, or an IV infusion. Giving ipilimumab this way is called an infusion because it allows the treatment to mix directly with the blood.

The ipilimumab doses in the trial were given in milligrams per kilogram, also known as mg/kg, of body weight.

The chart below shows the treatments the patients could get in Part 1:

Approved ipilimumab dose	3 mg/kg in an IV
Trial ipilimumab dose	10 mg/kg in an IV

For Part 1, the researchers used a computer program to randomly choose the treatment each patient got. Each patient had the same chance of getting one treatment or the other. This helped make sure that there was a similar number of patients in each treatment group.

If the patients' tumors stayed the same or got smaller after Part 1, the patients could continue into Part 2. The patients who continued into Part 2 kept getting the same ipilimumab dose that they got in Part 1.

The patients who did not continue into Part 2 could keep getting the standard treatment for their cancer.

What happened during the trial?

Before the trial started, the patients visited the trial site for a screening visit to see if they could join the trial. During the screening visit, the researchers:

- did a full physical exam to see if the patients could join the trial
- checked the height, weight, blood pressure, heart rate, breathing rate, and temperature of the patients
- asked about the medical history of the patients, how they were feeling, and what medicines they were taking
- took blood and urine samples
- studied the patients' tumors

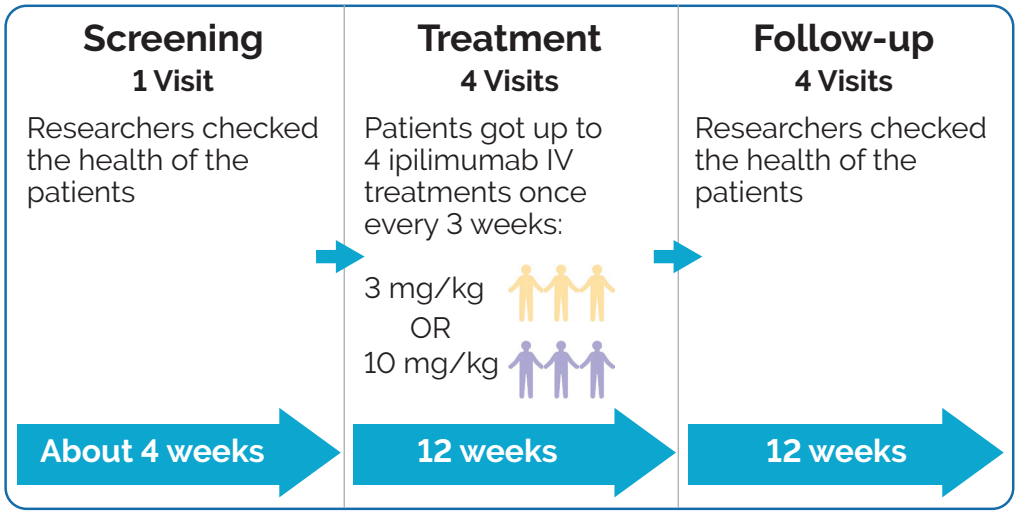
Throughout both parts of the trial, the researchers checked the overall health of the patients and took more blood and urine samples. The patients also filled out forms to report how they were feeling.

To see how the treatment was acting, researchers continued to do scans of the patients' tumors to see how the tumors were changing.

During Part 1:

- The patients visited their trial site up to 4 times. These visits happened once every 3 weeks over a 12-week period. During these 4 visits, the patients got an infusion of either 3 mg/kg or 10 mg/kg of ipilimumab.
- After 12 weeks of treatment, the patients visited their trial site 4 more times for follow-up visits so the researchers could check their health again.

The chart below shows what happened during Part 1 of the trial:

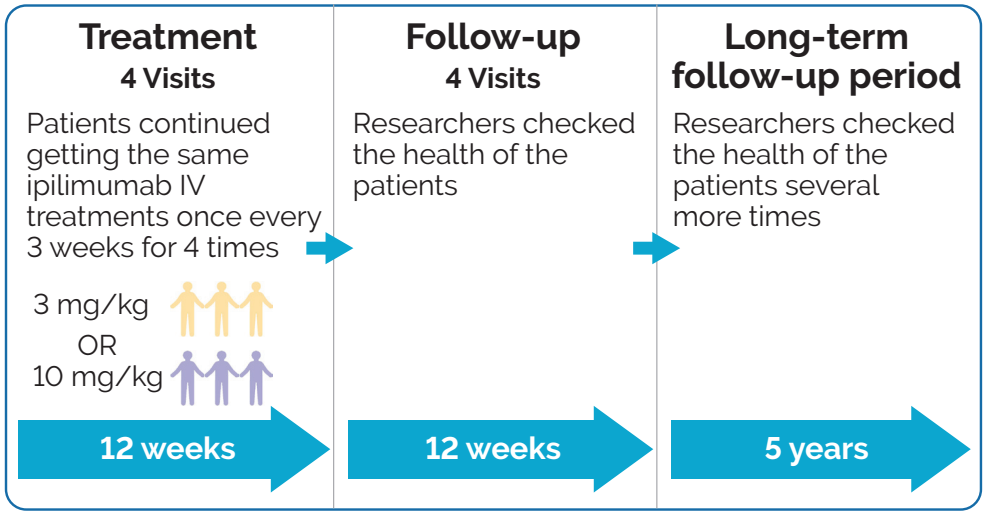


If the patients' tumors stayed the same or got smaller after the 12-week follow-up period in Part 1, the patients could continue into Part 2 of the trial.

During Part 2:

- The patients continued getting the same ipilimumab dose they got in Part 1.
- The patients visited their trial site up to 4 times. These visits happened once every 3 weeks over a 12-week period. During these 4 visits, the patients got an infusion of either 3 mg/kg or 10 mg/kg of ipilimumab.
- After 12 weeks of treatment, the patients visited their trial site 4 more times for follow-up visits so the researchers could check their health again.
- After the follow-up visits, the researchers checked the health of the patients over the course of about 5 years.

The chart below shows what happened during Part 2 of the trial:



What were the results of the trial?

This is a summary of the main results from the trial. The individual results each patient had might be different and are not in this summary. Always talk to a doctor before making any treatment changes.

Did the patients who got the trial dose of ipilimumab live longer than the patients who got the approved dose?

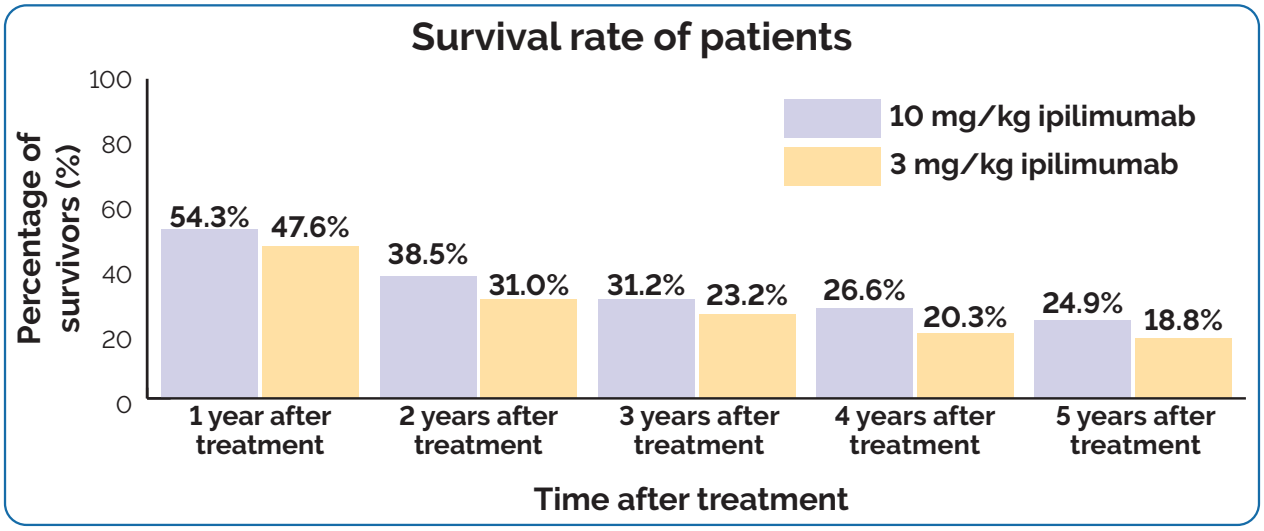
Yes. In general, the patients in the 10 mg/kg ipilimumab treatment group lived longer than the patients in the 3 mg/kg ipilimumab treatment group.

To answer this question, the researchers recorded how many patients survived 1, 2, 3, 4, and 5 years after they got treatment during the trial.

In general, the researchers found that:

- **After 1 year,** 54.3% of patients in the 10 mg/kg treatment group were still alive, compared to 47.6% of patients in the 3 mg/kg treatment group.
- **After 2 years,** 38.5% of patients in the 10 mg/kg treatment group were still alive, compared to 31.0% of patients in the 3 mg/kg treatment group.
- **After 3 years,** 31.2% of patients in the 10 mg/kg treatment group were still alive, compared to 23.2% of patients in the 3 mg/kg treatment group.
- **After 4 years,** 26.6% of patients in the 10 mg/kg treatment group were still alive, compared to 20.3% of patients in the 3 mg/kg treatment group.
- **After 5 years,** 24.9% of patients in the 10 mg/kg treatment group were still alive, compared to 18.8% of patients in the 3 mg/kg treatment group.

The chart below shows these results.



Did ipilimumab affect the patients in other ways?

In general, the researchers found that:

- It took a similar amount of time before the tumors grew for patients in both treatment groups.
- A similar percentage of patients in both treatment groups had their tumors disappear, shrink, or stay the same.
- It took 16.3 months for patients' tumors to change in the 10 mg/kg ipilimumab treatment group.
- It took 15.9 months for patients' tumors to change in the 3 mg/kg ipilimumab treatment group.
- It took 5.6 months for patients' tumors to change significantly in the 10 mg/kg ipilimumab treatment group.
- It took 3.2 months for patients' tumors to change significantly in the 3 mg/kg ipilimumab treatment group.

Did ipilimumab affect quality of life?

Researchers wanted to learn if ipilimumab helped improve the quality of life of patients. So, they gave patients surveys that asked them to rate how they were feeling at the end of treatment compared to at the beginning of the trial.

In general the researchers found that at the end of treatment, more patients in the 10 mg/kg ipilimumab treatment group felt worse than the patients in the 3 mg/kg ipilimumab treatment group did.

What medical problems did the patients have?

This section is a summary of the medical problems the patients had during the trial that the doctors thought might be related to the treatments. These medical problems are called "adverse reactions". An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or requires hospital care.

These adverse reactions may or may not be caused by the treatments in the trial. The results from several trials are needed to decide if a treatment causes an adverse reaction.

One of the patients left the trial before the researchers could collect all of the data for the trial, so the researchers could only study the medical problems for 726 of the 727 patients.

How many patients had serious adverse reactions?

There were 28.8% of patients who had serious adverse reactions during the trial.

This was 209 out of 726 patients. Serious adverse reactions happened more often in the patients in the 10 mg/kg ipilimumab treatment group compared to the patients in the 3 mg/kg ipilimumab treatment group.

The table below shows the serious adverse reactions that happened in at least 2.0% of patients in either treatment group during the trial. There were other serious adverse reactions, but these happened in fewer patients.

Most common serious adverse reactions during the trial

	Ipilimumab 10 mg/kg (Out of 364 patients)	Ipilimumab 3 mg/kg (Out of 362 patients)
Diarrhea	11.3% (41 patients)	5.5% (20 patients)
Swelling in the digestive system	9.1% (33 patients)	3.3% (12 patients)
Swelling in the glands (part of the body that controls hormones)	4.4% (16 patients)	2.2% (8 patients)

In the trial overall, there were 0.8% of patients who died because of adverse reactions during the trial. This was 6 out of 726 patients.

In the 10 mg/kg ipilimumab treatment group, there were 1.1% of patients who died because of adverse reactions during the trial. This was 4 out of 364 patients.

In the 3mg/kg ipilimumab treatment group, there were 0.6% of patients who died because of adverse reactions during the trial. This was 2 out of 362 patients.

How many patients had adverse reactions?

There were 71.8% of patients who had adverse reactions during the trial. This was 521 out of 726 patients. This happened more often in the patients in the 10 mg/kg ipilimumab treatment group compared to the patients in the 3 mg/kg ipilimumab treatment group.

There were 16.8% of patients who stopped taking treatments because of adverse reactions during the trial. This was 122 out of 726 patients. This happened more often in the patients in the 10 mg/kg ipilimumab treatment group compared to the patients in the 3 mg/kg ipilimumab treatment group.

What adverse reactions did the patients have?

The most common adverse reaction was diarrhea. This happened more often in the patients in the 10 mg/kg ipilimumab treatment group compared to the patients in the 3 mg/kg ipilimumab treatment group.

The adverse reactions below happened in 10.0% or more of patients in either treatment group during the trial. There were other adverse reactions, but these happened in fewer patients.

Most common adverse reactions during the trial

	Ipilimumab 10 mg/kg (Out of 364 patients)	Ipilimumab 3 mg/kg (Out of 362 patients)
Diarrhea	39.0% (142 patients)	23.5% (85 patients)
Rash	26.1% (95 patients)	14.6% (53 patients)
Itchy skin	22.8% (83 patients)	23.5% (85 patients)
Tiredness	11.3% (41 patients)	9.9% (36 patients)
Swelling in the digestive system	10.7% (39 patients)	5.5% (20 patients)

How has this trial helped patients and researchers?

The results from several trials are needed to decide which treatments work best and are safest. This summary shows only the main results from this one trial. Other trials may provide new information or different results.

The results of this trial helped researchers learn more about how the trial dose of ipilimumab acts and how safe it for people who have advanced melanoma tumors. The results may also be used in other trials to compare this drug with other treatments.

Further clinical trials with ipilimumab are planned.

Where can I learn more about the trial?

You can find more information about this trial on the websites listed below. If a full report of the trial's results is available, it might be on these websites:

- www.clinicaltrials.gov/ct2/show/study/NCT01515189
- www.clinicaltrialsregister.eu/ctr-search/search?query=CA184169

Full Trial Title: A Randomized Double-Blind Phase III Study of Ipilimumab Administered at 3 mg/kg vs at 10 mg/kg in Subjects with Previously Treated or Untreated Unresectable or Metastatic Melanoma

Protocol number: CA184169 (Checkmate 742)

National Clinical Trial number: NCT01515189

EudraCT number: 2011-004029-28

Bristol-Myers Squibb sponsored this trial and has its headquarters at [insert address]. The phone number for general information is [insert phone number].

Thank you

Patients in clinical trials 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 and caregivers.

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 participants for clinical trials, nor is it involved in conducting clinical trials.

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