CLINICAL TRIAL RESULTS

Researchers look at the results of many studies to decide which treatments may offer patients improvements in terms of efficacy and safety. It takes people taking part in many studies around the world to help researchers decide this. This summary only shows the results from this study. Other studies might have different results.

Sponsor	BeiGene, Ltd.
Medicine(s) Studied	Tislelizumab
Protocol Number	BGB-A317-301
Dates of Study	December 2017 to December 2023
Title of This Study	A Study of Tislelizumab Versus Sorafenib in Participants with Unresectable Hepatocellular Carcinoma (HCC)
Date of This Report	September 2024

Thank You!

BeiGene, who managed this study, thanks participants for taking part in the clinical study for a new medical treatment called tislelizumab. In this study, researchers learned more about the safety and efficacy of tislelizumab, also called BGB-A317, and how it may work in patients with a type of cancer called hepatocellular carcinoma (HCC).

BeiGene thinks it is important to share the results of the study with the public. If you participated in the study and have questions about the results, please speak with the doctor or staff at your study center.

Why was this study done?

Researchers are looking for better ways to help people with different types of cancer, including hepatocellular carcinoma (HCC). HCC begins in the liver, the body's largest internal organ that plays an important role in filtering toxins and producing bile to help with digestion. It is an aggressive cancer often linked to chronic liver disease or cirrhosis, conditions that can result from hepatitis infection, excessive alcohol consumption, or fatty liver disease. In its early stages, HCC may not cause noticeable symptoms, making early detection difficult. As it progresses, individuals may experience abdominal pain, weight loss, jaundice, or swelling in the abdomen. Advanced HCC can impact liver function and spread to nearby organs, requiring immediate medical care and special treatments.

In this study, researchers wanted to learn how safe and helpful tislelizumab is for patients with HCC when compared to another drug called sorafenib that is often used to treat this type of cancer. Tislelizumab helps the immune system fight cancer by blocking PD-1, which stands for Programmed Cell Death Protein 1. PD-1 is a protein on immune cells that acts as a brake, preventing them from attacking nearby cells. This is important for protecting healthy cells, but cancer cells can use PD-1 to hide from the immune system. By blocking PD-1, tislelizumab helps immune cells recognize and attack cancer cells.

Sorafenib is a medication that helps fight cancer by blocking certain proteins that cancer cells use to grow and form new blood vessels. One of these proteins is called VEGFR, which stands for Vascular Endothelial Growth Factor Receptor. VEGFR helps cancer cells create their own blood supply, which they need to get nutrients and grow. Sorafenib also blocks other proteins, like RAF kinases, which are involved in cell growth. By targeting these pathways, sorafenib works to slow down the growth of cancer cells and slow their ability to spread. It is commonly used as a treatment for liver cancer that cannot be removed with surgery.

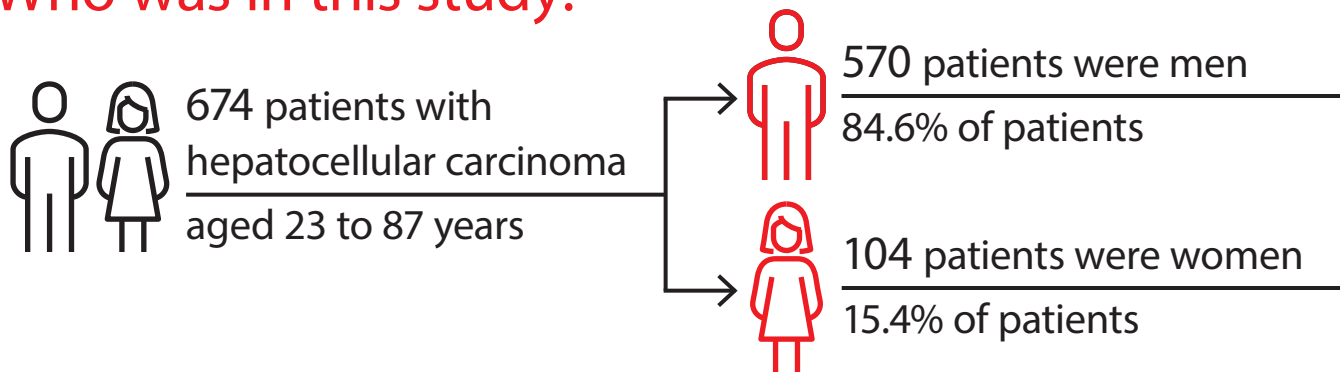
Before a new medical treatment can be approved for people to take, researchers must do clinical studies to learn how safe the treatment is by looking at adverse events, or side effects. Adverse events are unwanted medical problems that study participants can experience that may or may not be caused by the study drug. Researchers also must learn how the treatment works in people with the disease.

In this study, researchers compared tislelizumab to sorafenib for treating HCC.

Researchers in this study wanted to know:

- What adverse events would patients who took part in this study have?
- How long did patients participating in this study live after receiving this treatment?
- How long did patients participating in the study live without their cancer getting worse?
- How many people who took part in the study no longer had evidence of cancer or had some improvement in the signs and symptoms of active disease?

Who was in this study?



When and where was this study done?

This study started in December 2017 and ended in December 2023. The study was done at 107 study centers in 11 countries, including:

- Mainland China, with 411 patients
- Czech Republic, with 3 patients
- France, with 50 patients
- Germany, with 19 patients
- Italy, with 37 patients
- Japan, with 77 patients
- Poland, with 19 patients
- Spain, with 15 patients
- Taiwan, with 14 patients
- United Kingdom, 10 patients
- United States, with 19 patients

How was this study done?

In this study, patients with HCC were randomly assigned to one of two groups. One group received only tislelizumab, while the other group was only given a comparison treatment called sorafenib. Patients in the tislelizumab group received 200 milligrams of the drug through an intravenous (IV) line once every 3 weeks, continuing until they could no longer tolerate it, chose to stop, or their doctor decided the treatment was not effective. Patients in the sorafenib group took a 400 mg tablet of sorafenib by mouth twice daily, also continuing until they could no longer tolerate it, decided to stop, or their doctor determined it was no longer effective. Randomly placing patients in each group helps ensure the groups are as similar as possible, allowing researchers to fairly compare the outcomes of each treatment.

342 patients
were assigned to the
tislelizumab treatment group

Patients received
tislelizumab intravenously at

200 mg

ONCE EVERY 3 WEEKS

332 patients
were assigned to the
sorafenib treatment group

Patients received
sorafenib orally at

400 mg

TWICE DAILY

During this study, the doctors:

- Checked patients' overall health and took blood and urine samples
- Asked patients how they were feeling and what medicines they were taking
- Asked patients how well they could move and do their daily activities
- Tested how well patients could see with a vision test
- Measured how well patients' hearts were using an electrocardiogram machine
- Took images of patients' bodies with an X-ray machine to determine the tumor's status
- Collected samples of fresh tumor tissue from patients.

What adverse events did patients have?

Adverse events are medical problems that may or may not be caused by the study treatment. An adverse event is called "serious" if it causes long-lasting problems, puts the patient in the hospital, is life-threatening, is considered medically important by the study researcher, or leads to death. A total of 674 patients received at least one dose of study drug and were assessed for adverse events.

Below are the adverse events that patients had in this study. The websites listed at the end of this summary may have more information about the adverse events that occurred in this study.

In this study:

- 96.2% of patients in the tislelizumab group and 100% of patients in the sorafenib group had at least 1 adverse event
- 30.8% of patients in the tislelizumab group and 28.1% of patients in the sorafenib group had a serious adverse event
- 11.5% of patients in the tislelizumab group and 18.5% of patients in the sorafenib group had adverse events that caused them to stop the treatment.

What serious adverse events did patients have?

An increase in aspartate aminotransferase (AST), which is an enzyme in the blood that usually signals liver or muscle damage, was the most common serious side effect in this study, affecting at least 1% of patients.

Serious adverse event	Tislelizumab (338 patients)	Sorafenib (324 patients)
Ascites (build-up of fluid in the belly)	1.2% (4 Patients)	1.2% (4 Patients)
Bleeding in the upper digestive tract	1.2% (4 Patients)	0.3% (1 Patient)
Abdominal Pain	0.6% (2 Patients)	1.2% (4 Patients)
Liver failure	1.2% (4 Patients)	0.9% (3 Patients)
Jaundice (yellowing of skin and eyes)	0.9% (3 Patients)	1.5% (5 Patients)
AST Increased (elevated liver enzyme levels)	1.8% (6 Patients)	1.5% (5 Patients)
Alanine aminotransferase increased (elevated liver enzyme levels)	1.5% (5 Patients)	1.2% (4 Patients)
Pneumonia (lung infection)	1.5% (5 Patients)	0.9% (3 Patients)
Fever	0.9% (3 Patients)	1.5% (5 Patients)
Overall health decline	0.3% (1 Patient)	1.2% (4 Patients)
Shortness of breath	0% (0 Patients)	1.2% (4 Patients)

A total of 16 patients (4.7%) in the tislelizumab group and 17 (5.2%) in the sorafenib group had adverse events that led to death. Three (0.9%) of the adverse events leading to death in the tislelizumab group and 2 (0.6%) in the sorafenib group were possibly related to the study treatments.

What were the most common adverse events?

Liver enzyme increases in the blood was the most common adverse event in both groups. The most common side effect (adverse event) that occurred in at least 20% of the patients in this study are shown here.

Adverse event	Tislelizumab (338 patients)	Sorafenib (324 patients)
Aspartate aminotransferase increased (liver enzyme increase)	37.9% (128 Patients)	42.3% (137 Patients)
Alanine aminotransferase increased (liver enzyme increase)	28.7% (97 Patients)	35.2% (114 Patients)
Platelet count decreased (lower number of blood cells that help with clotting)	14.8% (50 Patients)	21.3% (69 Patients)
Diarrhoea	11.2% (38 Patients)	43.8% (142 Patients)
High blood pressure	6.8% (23 Patients)	27.8% (90 Patients)
Hair Loss	0.6% (2 Patients)	23.1% (75 Patients)
Palmar-plantar erythrodysaesthesia syndrome (Pain, redness, and swelling in the hands and feet)	0.3% (1 Patient)	62.7% (203 Patients)

What were the main results of the study?

Below is a summary of the main results of this study. The results for each patient in the study are not shown here and may be different from the overall results shown below.

You can find a full list of the questions for this study on the websites listed on the last page of this summary. If results are already available, they will also be found on these websites.

How long did patients participating in this study live after receiving treatment?

Measuring **overall survival** is one way to determine how well a new cancer treatment works. Overall survival is the median amount of time that patients live after the start of treatment. Median is the middle number in a group of numbers. In this study, some patients lived for a shorter time, and some lived longer. After a median follow up time of approximately 42 months, patients in the tislelizumab group lived a median of about 16 months. Patients in the sorafenib group lived about 14 months. A total of 674 patients were part of this analysis.

How long do patients live without their cancer getting worse?

Researchers wanted to know how long patients survived without HCC getting worse after starting study treatment, also known as **progression free survival.** After a median follow-up time of 14 months, the median length of time that patients survived without HCC getting worse was 2.1 months in the tislelizumab group and 4 months for patients in the sorafenib group. Median is the middle number in a group of numbers.

How many people who took part in the study no longer had evidence of cancer or had some improvement in the signs and symptoms of active disease?

Measuring **overall response rate** is one way to determine how well a new cancer treatment works. The percentage of people with HCC who no longer had evidence of cancer or had some improvement in the signs and symptoms of active disease after treatment was 15.5% in the tislelizumab group and 5.7% in the sorafenib group after a median of 14 months follow-up.

How has this study helped patients and researchers?

The results from this study will help researchers understand more about how tislelizumab works in patients with HCC and may provide additional treatment options for patients in the future. More studies with tislelizumab are ongoing and planned.

The results in this summary come from this one study. Other studies may show different results. If you participated in this study and have questions about the results, please speak to the doctor or staff at your study center. You should not make changes to your treatments based on the results of this study.

Where can I found out more about this study?

More information about this study, including any available results, is found below:

The full title of this study is

RATIONALE-301: A Randomized, Open-label, Multicenter Phase 3 Study to Compare the Efficacy and Safety of BGB-A317 Versus Sorafenib as First-Line Treatment in Patients With Unresectable Hepatocellular Carcinoma.

The protocol number is

BGB-A317-301

For information about this study in the United States

Click here

For information about this study in the European Union

Click here

For information about this study in China

Click here

For information about this study from BeiGene

Click here

Clinical study participants help researchers make important discoveries that may lead to new medical treatments worldwide. BeiGene sponsored this study and is thankful for the help of the patients in this study.

For more information about BeiGene:

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BeiGene thanks all the participants for their time and effort that went into making this study possible. Clinical study participants help advance science!