Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine(s) Studied: Ontorpacept (previously known as TTI-621)

Protocol Number: C4961003

Dates of Study: 22 June 2021 to 07 December 2023

Title of this Study: A Study of Ontorpacept in Combination With Doxorubicin in Participants With Aggressive Soft Tissue Cancers

[A Phase I/II Study of TTI-621 in Combination With Doxorubicin in Patients With Unresectable or Metastatic High-Grade Leiomyosarcoma]

Date(s) of this Report: 26 July 2024

– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is leiomyosarcoma?

Leiomyosarcoma is a type of rare cancer that grows and spreads quickly in the soft tissues of the body. Soft tissues, like muscles, fat and blood vessels, are in the hollow organs of the body. Leiomyosarcoma can occur anywhere in the body. The symptoms depend on where the tumor occurs, causing cramping or pain.

What is ontorpacept?

Ontorpacept is the medicine used in this study. It is a type of protein that blocks a protein present on cancer cells, called CD47. This process may help the immune system of the body (the body's natural defences) to fight cancer. Ontorpacept was given as an infusion into the vein. In this study, ontorpacept was tested when given together with doxorubicin and then given alone. Different doses of ontorpacept were tested. Doxorubicin is a chemotherapy that has been used to treat people with aggressive soft tissue cancers.

What was the purpose of this study?

The primary goals of this study were:

- to find the highest dose of ontorpacept that participants can tolerate, when given in combination with doxorubicin and then given alone
- to learn about the safety of ontorpacept when given in combination with doxorubicin and then given alone, until disease worsening
- to find out the percentage of participants whose cancer has been cured completely or partially decreased in the extent, after treatment with ontorpacept when given in combination with doxorubicin and then given alone

Researchers wanted to know:

- **What was the highest dose of ontorpacept that participants can tolerate given in combination with doxorubicin?**
- **How safe was ontorpacept given in combination with doxorubicin and then given alone?**
- **What was the percentage of participants whose cancer has been cured completely or partially decreased in the extent, after treatment with ontorpacept given in combination with doxorubicin and then given alone?**

What happened during the study?

How was the study done?

This study was done in 2 phases, as shown in figure 1 below.

Phase 1

In phase 1, researchers wanted to find the highest dose of ontorpacept that participants could tolerate when given in combination with doxorubicin in participants with aggressive soft tissue cancer. The participants received different doses of ontorpacept (0.2 mg/kg, 0.7 mg/kg and 2.0 mg/kg) in combination with doxorubicin 75 mg/m^2, for 18 weeks and then, they continued to receive ontorpacept alone until they leave the study.

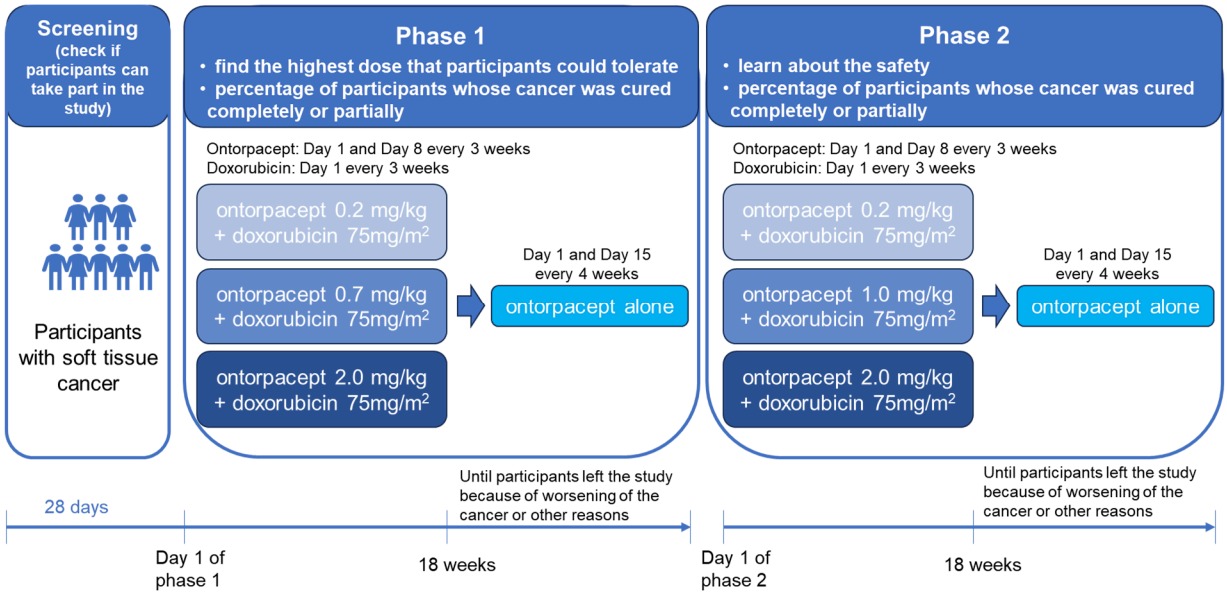
For each different dose, researchers checked if participants had any medical problems which usually prevent further increases in the dose of the study medication. This was done before deciding if participants could receive a higher dose of the study medication.

Phase 2

In phase 2, researchers wanted to learn about the safety of ontorpacept given in combination with doxorubicin and then given alone, in participants with aggressive soft tissue cancers, until disease worsening. The participants received different doses of ontorpacept (0.2 mg/kg, 1.0 mg/kg and 2.0 mg/kg) in combination with doxorubicin 75 mg/m^2, and then, they continued to receive ontorparcept alone until they leave the study.

In both phase 1 and phase 2, the researchers wanted to find out the percentage (%) of participants whose cancer has been cured completely or partially decreased in the extent, after treatment with ontorpacept when given in combination with doxorubicin and then given alone.

Figure 1: What happened during the study



The study participants and researchers knew what medication the participants took. This is known as an “open-label” study.

Where did this study take place?

The Sponsor ran this study at 11 locations in the United States of America.

When did this study take place?

It began on 22 June 2021 and ended on 07 December 2023.

Who participated in this study?

The study included participants who were diagnosed with aggressive soft tissue cancers with no possible treatment with surgery or radiation. Participants should not have more than 1 previous treatment for their disease.

- A total of 21 men participated.
- A total of 55 women participated.
- All participants were between the ages of 25 and 77 years.

Of the 76 participants who started the study (9 in phase 1 and 67 in phase 2), all were treated with ontorpacept in combination with doxorubicin.

In phase 1, 3 participants received ontorpacept 0.2 mg/kg, 3 participants received ontorpacept 0.7 mg/kg, and 3 participants received ontorpacept 2.0 mg/kg.

In phase 2, 32 participants received ontorpacept 0.2 mg/kg, 13 participants received ontorpacept 1.0 mg/kg, and 22 participants received ontorpacept 2.0 mg/kg.

How long did the study last?

The entire study took about 2.5 years. The study was early terminated by the Sponsor for administrative reasons.

When the study ended in December 2023, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

- **What was the highest dose of ontorpacept that participants could tolerate when given in combination with doxorubicin?**

None of the participants had medical problems which prevented the increase in the dose of ontorpacept. The highest dose of ontorpacept when given with doxorubicin that participants could tolerate was not determined in this study.

- **How safe was ontorpacept given in combination with doxorubicin and then given alone?**

Both phase 1 and phase 2 of this study showed that ontorpacept in combination with doxorubicin was generally tolerable and the unpleasant effects were manageable.

- **What was the percentage of participants whose cancer has been cured completely or partially decreased in the extent, after treatment with ontorpacept given in combination with doxorubicin and then given alone?**

There were no participants whose cancer has been cured completely after treatment.

In phase 1, 1 out of 3 (33%) participants treated with ontorpacept 2.0 mg/kg in combination with doxorubicin showed a decrease in the extent of the cancer after treatment.

In phase 2, 6 out of 32 (19%) participants treated with ontorpacept 0.2 mg/kg in combination with doxorubicin and 1 out of 22 (4%) participants treated with ontorpacept 2.0 mg/kg in combination with doxorubicin showed a decrease in the extent of the cancer after treatment.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused

by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

All (100%) participants in this study had at least 1 medical problem. Nine participants discontinued ontorpacept because of medical problems. Fifteen participants discontinued doxorubicin because of medical problems. Six participants discontinued both ontorpacept and doxorubicin because of medical problems. The most common medical problems – those reported by more than 15% of participants – are described below.

Below are instructions on how to read the Table(s).

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by more than 15% of participants are listed.
- The **2nd** column tells how many of the 9 participants taking ontorpacept in combination with doxorubicin in phase 1 reported each medical problem. Next to this number is the percentage of 6 participants taking the study medication who reported tiredness.
- Using these instructions, you can see that 6 out of the 9 [67%] participants taking ontorpacept in combination with doxorubicin reported tiredness, in phase 1.

Instructions for Understanding Table 2.

- The **1st** column of Table 2 lists medical problems that were commonly reported during the study. All medical problems reported by more than 15% of participants are listed.
- The **2nd** column tells how many of the 67 participants taking the ontorpacept in combination with doxorubicin in phase 2 reported each medical problem. Next to this number is the percentage of 46 participants taking the study medication who reported tiredness.
- Using these instructions, you can see that 46 out of the 67 [69%] participants taking ontorpacept combination with doxorubicin reported tiredness, in phase 2.

Table 1. Commonly reported medical problems by study participants, in phase 1 of the study

Medical Problem	Ontorpacept (all phase 1 participants) (9 Participants)
Tiredness	6 out of 9 participants (67%)
Feeling sick	6 out of 9 participants (67%)
Low levels of red blood cells	4 out of 9 participants (44%)
Headache	4 out of 9 participants (44%)
Vomiting	4 out of 9 participants (44%)

Table 1. Commonly reported medical problems by study participants, in phase 1 of the study	
Medical Problem	**Ontorpacept (all phase 1 participants) (9 Participants)**
Low levels of neutrophils, a type of white blood cells	4 out of 9 participants (44%)
Reaction caused during or shortly after receiving a treatment by infusion	2 out of 9 participants (22%)
Inflammation of the lining of the mouth	2 out of 9 participants (22%)
Constipation	2 out of 9 participants (22%)
Cough	2 out of 9 participants (22%)
Diarrhoea	2 out of 9 participants (22%)
Infection of the parts of the body that collect and pass out urine	2 out of 9 participants (22%)
Difficulty breathing	2 out of 9 participants (22%)
Fever	2 out of 9 participants (22%)
Low levels of blood platelets (the components that help the blood to clot), which can lead to bleeding and bruising	2 out of 9 participants (22%)

Table 2. Commonly reported medical problems by study participants, in phase 2 of the study	
Medical Problem	**Ontorpacept (all phase 2 participants) (67 Participants)**
Tiredness	46 out of 67 participants (69%)
Feeling sick	43 out of 67 participants (64%)
Low levels of red blood cells	39 out of 67 participants (58%)
Decrease in platelet (the components that help the blood to clot) count	39 out of 67 participants (58%)
Decreased neutrophil (a type of white blood cells) count	35 out of 67 participants (52%)
Reaction caused during or shortly after receiving a treatment by infusion	34 out of 67 participants (51%)
Hair loss	27 out of 67 participants (40%)
Decrease in white blood cell count	26 out of 67 participants (39%)
Headache	24 out of 67 participants (36%)
Inflammation of the lining of the mouth	23 out of 67 participants (34%)
Constipation	21 out of 67 participants (31%)

Table 2. Commonly reported medical problems by study participants, in phase 2 of the study	
Medical Problem	**Ontorpacept (all phase 2 participants) (67 Participants)**
Vomiting	15 out of 67 participants (22%)
Cough	15 out of 67 participants (22%)
Diarrhoea	14 out of 67 participants (21%)
Feeling dizzy	14 out of 67 participants (21%)
Low levels of neutrophils, a type of white blood cells	13 out of 67 participants (19%)
Infection of the parts of the body that collect and pass out urine	13 out of 67 participants (19%)
Decreased appetite	13 out of 67 participants (19%)
Decreased lymphocytes (a type of white blood cells) count	12 out of 67 participants (18%)
Difficulty breathing	11 out of 67 participants (16%)

Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

Thirty-four out of 76 (45%) participants had serious medical problems.

- In phase 1, 2 out of 9 (22%) participants had at least one serious medical problem. The serious medical problems were heart stops beating, heart attack, formation of blood clots in the veins in the upper arm, and formation of blood clots in the vein that carries blood from the right upper body.
- In phase 2, 32 out of 67 (48%) participants had at least one serious medical problem. The most common serious medical problems were low levels of white blood cells with fever and body's extreme reaction to an infection.

Twenty-seven out of 76 (36%) participants died during the study, most commonly due to disease under study. Four out of 9 (44%) deaths occurred in phase 1 and 23 out of 67 deaths (34%) in phase 2. Researchers do not believe any of the deaths were related to the study medication.

Where can I learn more about this study?

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

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C4961003

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT04996004**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!