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 (PF-07901800, TTI-621)

Protocol Number: C4961001

Dates of Study: 28 January 2016 to 23 November 2022

Title of this Study: A Study Looking at the Safety of Ontorpacept in Participants with Different Types of Cancers

[A Phase 1a/1b Dose Escalation and Expansion Trial of TTI-621, a Novel Biologic Targeting CD47, in Subjects With Relapsed or Refractory Hematologic Malignancies and Selected Solid Tumors]

Date of this Report: 13 November 2023

– 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 hematologic malignancy and solid tumor?

The study included participants with advanced hematologic malignancies or solid tumors. It had 4 parts: Part 1, Part 2, Part 3, and Part 4.

Hematologic malignancy also called as blood cancer is a type of cancer that affects the blood cells or the cells of the immune system (the body's natural defenses).

Solid tumor is a type of cancer that affects parts of the body like the bladder, breast, colorectal area (part of the intestines), head and neck, lung, pancreas, prostate, or ovary.

Part 1 and Part 2:

Participants in Part 1 had lymphomas, a type of cancer that generally develops in the lymph nodes and lymphatic tissue found in organs such as the stomach, intestines, skin, and sometimes bone marrow and blood. Participants had an "advanced relapsed or refractory" lymphoma that responds to initial treatment but returns or does not respond to the initial treatment.

In Part 2, participants who had advanced malignancy of the following types of blood cancers and solid tumors were selected: Aggressive B-cell lymphoma (ABCL), indolent B-cell lymphoma (IBCL), and T-cell lymphoma (TCL) are types of cancers that affects cells in the immune system such as B-cells and T-cells. Myelodysplastic syndrome (MDS) is a condition when the bone marrow does not make healthy blood cells. Acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), Hodgkin lymphoma (HL), classic Hodgkin lymphoma (cHL), chronic lymphocytic leukemia (CLL), multiple myeloma (MM), and myeloproliferative neoplasms (MPN)

are all different types of blood cancers. Small cell lung cancer (SCLC) is a type of solid tumor.

Participants in Part 3 had relapsed or refractory cutaneous T-cell lymphoma (CTCL) and peripheral T-cell lymphoma (PTCL). In Part 4 participants had relapsed or refractory CTCL.

What is ontorpacept?

Ontorpacept is a new investigational drug. It is not currently approved for use in any country. Researchers are testing ontorpacept in the treatment of cancer. Participants received ontorpacept as an infusion in a vein of the arm.

Ontorpacept is a type of protein that is designed to target and block a kind of protein on the cell surface called CD47. CD47 is present on cancer cells and some normal cells in the body. Cancer cells use this protein to hide from body's immune system. It is thought that blocking CD47 may help the immune system to fight cancer.

The majority of participants in this study received ontorpacept alone, and one cohort with participants who had cancer with a protein marker called CD20 was treated with ontorpacept plus rituximab. Similarly, a cohort of participants with cHL, a cancer that affects the lymphatic system of the body's immune system was treated with ontorpacept plus nivolumab to characterize the safety and efficacy of these two combinations.

Rituximab and nivolumab have been approved for treating specific types of cancers described, both are intravenous (IV) treatments.

What was the purpose of this study?

This study looked at the safety and tolerability of ontorpacept in participants with different type of blood cancers and solid tumors. "Tolerability" refers to how well participants can tolerate receiving the drug.

This was the first-time participants received ontorpacept. Researchers wanted to find out what the best and safest ("optimal") dose of the drug was to be administered. This will help them decide the dose that the participants could receive in future studies.

Assigned participants received increasing doses of ontorpacept (dose escalation). At each dose level, researchers checked if participants had whether or not any dose limiting toxicities (DLTs), before deciding if participants could receive higher dose in the next dose level. They also looked at the general safety of different doses.

DLTs are medical problems which usually prevent further increases in the dose of the study medication.

In Part 1 and Part 4 participants with relapsed or refractory hematologic malignancies and solid tumors received increasing doses of ontorpacept. In Parts 2 and 3 researchers tested ontorpacept in participants with different types of blood cancers and solid tumors to evaluate the safety of individual participants' ontorpacept dose intensification and potential to be studied further. This helped researchers to decide the best dose that the participants could receive with this type of cancers in future studies.

Researchers wanted to know:

- **How safe and well tolerated ontorpacept was?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

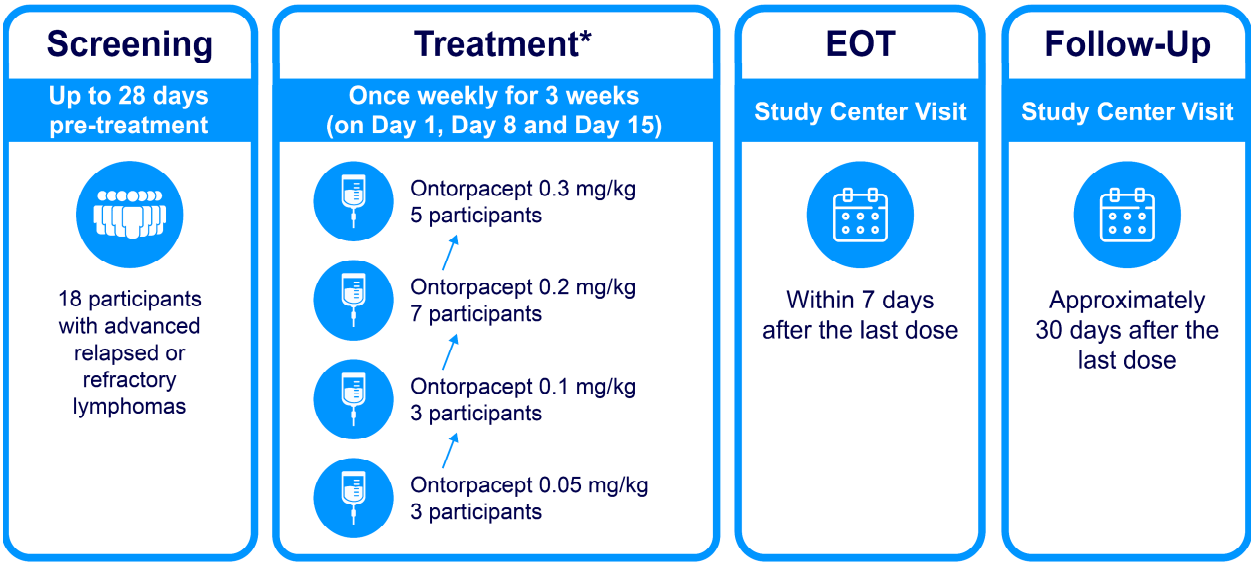
This was an “open-label” study. This means researchers and participants knew what study medication the participants received.

The study schemas for Part 1, Part 2, Part 3, and Part 4 are shown in Figure 1, 2, 3, and 4, respectively. All participants were “screened” to see if they qualified to be in the study. Participants had an End of Treatment (EOT) visit and a follow-up visit during the study.

Part 1

In Part 1, participants were treated in a cohort size of 3 participants starting at the 0.05 mg/kg dose level following a 3+3 design: if a DLT occurred in 1 of 3 participants within a cohort dose level in 21-day period, 3 additional participants were treated at that dose level. In the absence of DLT, enrolment proceeded sequentially through the planned dose levels. If DLT occurred in more than 1 out of 3/6 participants in a 21-day period, dose escalation was stopped.

Figure 1. Study Design for Part 1

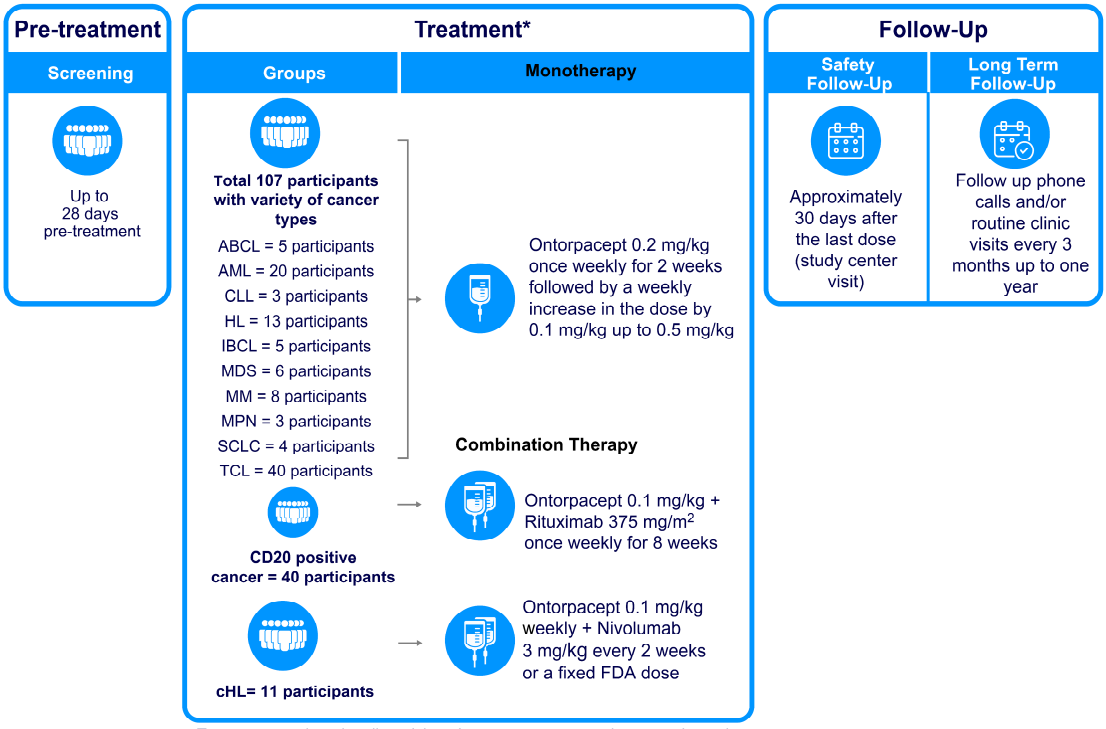


**Treatment continued until participant's cancer got worse, they experienced unacceptable medical problems, or they decided to stop treatment for other reasons*

Part 2

In Part 2, participants were treated with ontorpacept alone (monotherapy) or in combination with rituximab or nivolumab as shown in Figure 2. The starting dose of ontorpacept in Parts 2 and 3 was decided based on the results of Part 1.

Figure 2. Study Design for Part 2



** Treatment continued until participant's cancer got worse, they experienced unacceptable medical problems, or they decided to stop treatment for other reasons.*

Monotherapy cohorts: Each group of participants received a single starting dose of 0.2 mg/kg once weekly for first two weeks. The dose of ontorpacept was increased up to a dose of 0.5 mg/kg within 5-8 weeks by adding 0.1 mg/kg every week to the prior dose.

Combination cohorts: Researchers tested ontorpacept 0.1 mg/kg together with rituximab 375 mg/m^2 in participants who had CD20 positive cancers. Participants received ontorpacept in combination with rituximab once weekly (1 cycle) for up to 8 cycles. Participants who completed all the 8 cycles received ontorpacept as a single dose.

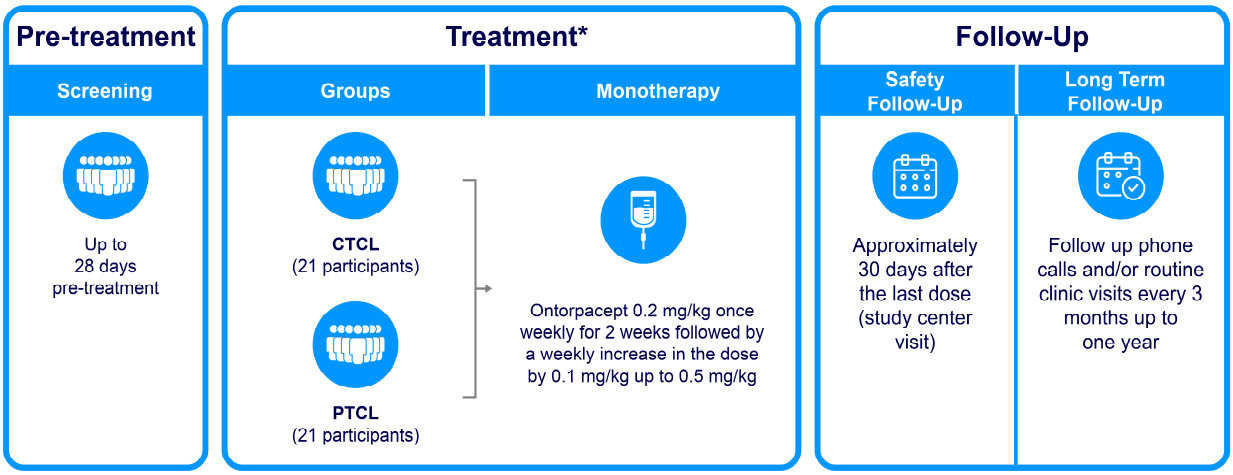
Researchers also tested ontorpacept 0.1 mg/kg together with nivolumab 3 mg/kg in participants who had cHL. Participants received ontorpacept once weekly with nivolumab every 2 weeks or a fixed dose as approved by

Food and Drug Administration (FDA) for cHL. Participants who experienced unacceptable medical problems received ontorpacept as a single dose.

Part 3

In Part 3 (Figure 3), participants received a single starting dose of ontorpacept 0.2 mg/kg once weekly for first two weeks. The dose of ontorpacept was increased up to a dose of 0.5 mg/kg within 5-8 weeks by adding 0.1 mg/kg every week to the prior dose.

Figure 3. Study Design for Part 3



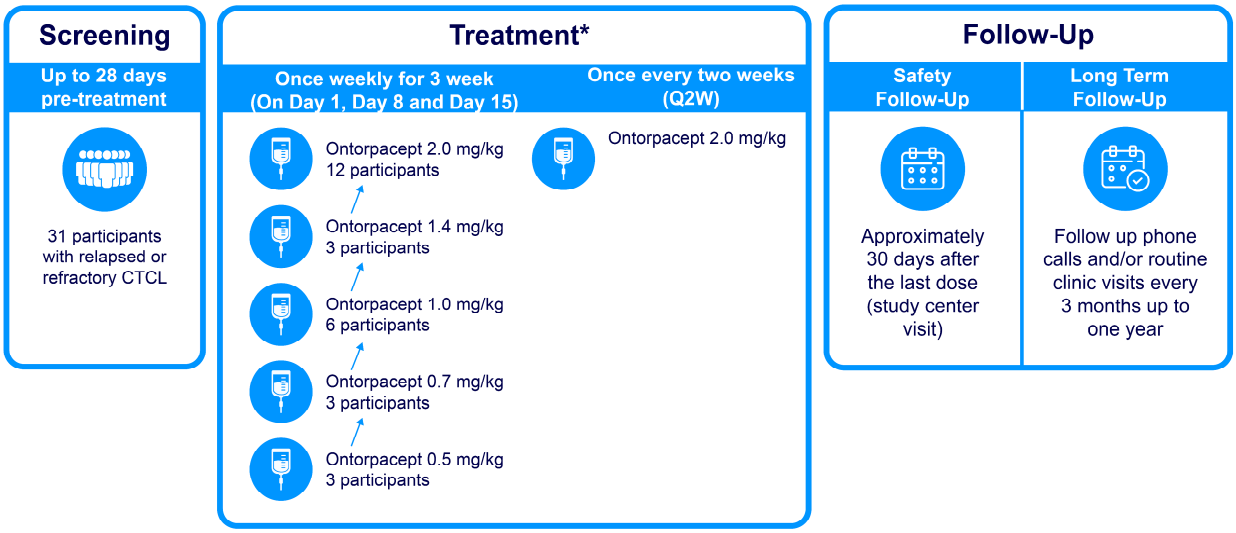
**Treatment continued until participant's cancer got worse, they experienced unacceptable medical problems, or they decided to stop treatment for other reasons*

Part 4:

Researchers further assessed the safety and tolerability of ontorpacept at higher dose levels in Part 4 of this study. The starting dose was 0.5 mg/kg once weekly based on the results from Parts 2 and 3 of this study. Participants received 2.0 mg/kg once weekly as the highest dose. Besides escalating doses, participants also received ontorpacept 2.0 mg/kg separately once every two weeks (Q2W).

Similar to Part 1, for the dose escalation portion of Part 4, participants were treated with a cohort size of 3 following a 3+3 design.

Figure 4. Study Design for Part 4



**Treatment continued until participant's cancer got worse, they experienced unacceptable medical problems, or they decided to stop treatment for other reasons*

Where did this study take place?

The Sponsor ran this study at 18 locations in the United States and Canada.

When did this study take place?

It began on 28 January 2016 and ended on 23 November 2022.

Who participated in this study?

The study included participants who had relapsed or refractory hematologic malignancies or solid tumors.

Participants whose cancer has returned or worsened since the previous treatment or whose cancer has no further approved treatment were included in the study.

- A total of 153 men participated.
- A total of 96 women participated.
- All participants were between the ages of 21 and 87 years.

Of the 249 participants who started the study, 73 completed the study.

Part 1

Of the 18 participants who started Part 1 of the study, 1 participant who received ontorpacept 0.3 mg/kg completed the study. Other participants did not complete the study due to the following reasons:

- Participant's cancer got worse; (2 out of 3 participants in ontorpacept 0.05 mg/kg group), (3 out of 3 participants in ontorpacept 0.1 mg/kg group), (2 out of 7 participants in ontorpacept 0.2 mg/kg group), and (3 out of 5 participants in ontorpacept 0.3 mg/kg group).
- Withdrawal of informed consent; (1 participant each in ontorpacept 0.05 mg/kg group, ontorpacept 0.2 mg/kg group, and 0.3 mg/kg group).
- Death; (1 out of 7 participants in ontorpacept 0.2 mg/kg group).
- Lost to follow-up; (1 out of 7 participants in ontorpacept 0.2 mg/kg group).
- Other reasons; (2 out of 7 participants in ontorpacept 0.2 mg/kg group).

Part 2 and Part 3

In Part 2, out of 107 participants who received ontorpacept monotherapy 29 participants completed the study. The remaining participants did not complete the study due to the following reasons:

- Death; (50 out of 107 participants).

- Lost to follow-up; (4 out of 107 participants).
- Participant's cancer got worse; (2 out of 107 participants).
- Withdrawal of informed consent; (16 out of 107 participants).
- Other reasons; (6 out of 107 participants).

Of the 11 participants who received ontorpacept in combination with nivolumab, 10 participants completed the study. One participant (9.1%) stopped the treatment due to withdrawal of informed consent.

Of the 40 participants who received ontorpacept in combination with rituximab, 6 participants completed the study. Other participants did not complete the study due to the following reasons:

- Death; (25 out of 40 participants).
- Lost to follow-up; (3 out of 40 participants).
- Study closed by researcher; (1 out of 40 participants).
- Withdrawal of informed consent; (3 out of 40 participants).
- Other reasons; (2 out of 40 participants).

In Part 3, out of 42 participants who received ontorpacept monotherapy 15 participants (35.7%) completed the study. The remaining participants did not complete the study due to the following reasons:

- Death; (16 out of 42 participants).
- Lost to follow up; (3 out of 42 participants).
- Withdrawal of informed consent; (8 out of 42 participants).

Part 4

Of the 31 participants who started Part 4 of the study, 12 participants

completed the study. The remaining participants did not complete the study due to the following reasons:

- Participant's cancer got worse; (1 out of 3 participants in ontorpacept 1.4 mg/kg group).
- Withdrawal of informed consent; (2 out of 3 participants in ontorpacept 0.7 mg/kg group), (1 out of 3 participants in ontorpacept 1.4 mg/kg group), (1 out of 12 participants in ontorpacept 2.0 mg/kg group), and (1 out of 4 participants in ontorpacept Q2W/2.0 mg/kg group).
- Death; (2 out of 6 participants in ontorpacept 0.1 mg/kg group), (5 out of 12 participants in ontorpacept 2.0 mg/kg group), and (1 out of 4 participants in ontorpacept Q2W/2.0 mg/kg group).
- Lost to follow-up; (1 out of 12 participants in ontorpacept 2.0 mg/kg group).
- Other reasons; (1 out of 6 participants in ontorpacept 1.0 mg/kg group), (1 out of 3 participants in ontorpacept 1.4 mg/kg group), and (1 out of 4 participants in ontorpacept Q2W/2.0 mg/kg group).
- Study closed by researcher; (1 out of 12 participants in ontorpacept 2.0 mg/kg group).

How long did the study last?

The time participants were in the study, depended on their number of treatment cycles and follow-up time. The entire study took about 6 years, 9 months, and 26 days to complete.

Sponsor decided to close the study in September 2022 for administrative reasons. After the last participant who entered the study received their last dose in November 2022, the Sponsor created a report of the results. This is a summary of that report.

What were the results of the study?

How safe and well tolerated was ontorpacept?

Researchers looked at the medical problems that participants had after each dose of ontorpacept in Part 1 and Part 4 to see if there were DLTs. This helped researchers decide if each dose was safe and well tolerated, and if it was safe to the next group of participants to receive a higher dose of the drug.

Medical problems throughout the whole of the study are discussed in full in the next section of this document.

Did participants who received ontorpacept in Part 1 and Part 4 of the study have DLTs?

- In Part 1 of this study, 1 out of the 5 participants (20.0%) at ontorpacept 0.2 mg/kg dose and 2 out of the 5 participants (40.0%) at ontorpacept 0.3 mg/kg dose who were evaluable for DLTs, experienced medical problems that were considered to be DLTs as shown in Figure 5 below.

Figure 5: DLTs for Part 1

Ontorpacept 0.3 mg/kg 2 participants	Ontorpacept 0.3 mg/kg 1 participant each	Ontorpacept 0.2 mg/kg 1 participant
Low levels of platelets	• Alanine aminotransferase (ALT) liver test increased • Aspartate aminotransferase (AST) liver test increased	Low levels of phosphates

- In Part 4 of this study, 1 out of 6 participants (16.7%) at ontorpacept 1 mg/kg dose and 2 out of 7 participants (28.6%) at ontorpacept

2 mg/kg dose who were assessed for DLTs, experienced medical problems that were considered to be DLTs.

- One participant at ontorpacept 1 mg/kg dose experienced infusion related reaction (IRR). Medical problems related to infusion of the study medication are called “infusion-related reactions” or IRRs.
- One participant each at ontorpacept 2 mg/kg dose experienced low levels of white blood cells (WBC), low levels of neutrophils (a key type of WBC) and low levels of platelets

What was the maximum tolerated dose (MTD) of ontorpacept?

Researchers concluded that the MTD in Part 1 was reached at the dose level of 0.2 mg/kg. This dose was further tested in Parts 2 and 3 of the study. For dose optimization in Part 4, researchers concluded that ontorpacept was tolerated at the dose of 1.0 mg/kg and not tolerated at the dose of 2.0 mg/kg. Also, ontorpacept was not fully evaluated at the dose of 1.4 mg/kg.

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 receiving. Sometimes the cause of a medical problem is unknown. By comparing medical problems and the possible causes across study groups, doctors try to understand what effects a study medication might have on a participant.

Part 1

All participants had at least 1 “treatment-emergent” medical problem. “Treatment-emergent” medical problem is defined as any medical problem starting on or after the first date of treatment, up to 30 days post last date of treatment. No participants discontinued Part 1 treatment because of medical problems.

The most common medical problems – those reported by more than 10% of study participants in Part 1 – are described in Table 1.

Part 2 and Part 3

- In Part 2, a total of 103 out of 107 (96.3%) participants in ontorpacept monotherapy group had at least 1 treatment-emergent medical problem. All 11 (100.0%) participants in nivolumab combination group and 37 out of 40 (92.5%) participants in rituximab combination group also had at least 1 treatment-emergent medical problem. A total of 14 participants in monotherapy group, 1 participant in nivolumab combination group and 4 participants in rituximab combination group discontinued ontorpacept treatment because of medical problems.
- A total of 40 out of 42 (95.2%) participants in Part 3 had at least 1 treatment-emergent medical problem. Four participants discontinued ontorpacept treatment because of medical problems.
- The most common medical problems – those reported by more than 10% of study participants in Parts 2 and 3 – are described in Table 2.

Part 4

All participants had at least 1 “treatment-emergent” medical problem. A total of 2 participants at 1.0 mg/kg dose and 1 participant at 2.0 mg/kg dose discontinued ontorpacept treatment because of medical problems.

The most common medical problems – those reported by more than 10% of study participants in Part 4 – are described in Table 3.

Below are instructions on how to read Table 1, Table 2, and Table 3.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during Part 1 of the study. All medical problems reported by more than 10% of participants are listed.
- The **2nd** and **3rd** columns tell how many of the 3 participants receiving ontorpacept 0.05 mg/kg and ontorpacept 0.1 mg/kg reported each medical problem. Next to this number is the percentage of the 3 participants receiving ontorpacept 0.05 mg/kg and 0.1 mg/kg who reported the medical problem.
- The **4th** column tells how many of the 7 participants receiving ontorpacept 0.2 mg/kg reported each medical problem. Next to this number is the percentage of the 7 participants receiving ontorpacept 0.2 mg/kg who reported the medical problem.
- The **5th** column tells how many of the 5 participants receiving ontorpacept 0.3 mg/kg reported each medical problem. Next to this number is the percentage of the 5 participants receiving ontorpacept 0.3 mg/kg who reported the medical problem.
- Using these instructions, you can see that 2 out of the 3 (66.7%) participants receiving ontorpacept 0.05 mg/kg and 0.1 mg/kg, 4 out of the 7 (57.4%) participants receiving ontorpacept 0.2 mg/kg and 4 out of the 5 (80.0%) participants receiving ontorpacept 0.3 mg/kg reported IRR.

Instructions for Understanding Table 2.

- The **1st** column of Table 2 lists medical problems that were commonly reported during Part 2 and Part 3 of the study. All medical problems reported by more than 10% of participants are listed.
- The **2nd** column tells how many of the 107 participants receiving ontorpacept monotherapy in Part 2 reported each medical problem. Next to this number is the percentage of the 107 participants receiving ontorpacept monotherapy who reported the medical problem.
- The **3rd** column tells how many of the 42 participants receiving ontorpacept monotherapy in Part 3 reported each medical problem. Next to this number is the percentage of the 42 participants receiving ontorpacept monotherapy who reported the medical problem.
- The **4th** column tells how many of the 11 participants receiving ontorpacept together with nivolumab in Part 2 reported each medical problem. Next to this number is the percentage of the 11 participants receiving ontorpacept together with nivolumab who reported the medical problem.
- The **5th** column tells how many of the 40 participants receiving ontorpacept together with rituximab in Part 2 reported each medical problem. Next to this number is the percentage of the 40 participants receiving ontorpacept together with rituximab who reported the medical problem.
- Using these instructions, you can see that 46 out of the 107 (43.0%) participants receiving ontorpacept monotherapy in Part 2 of the study, 16 out of the 42 (38.1%) participants receiving ontorpacept monotherapy in Part 3 of the study,

5 out of the 11 (45.5%) participants receiving ontorpacept in combination with nivolumab, and 17 out of the 40 (42.5%) participants receiving ontorpacept in combination with rituximab reported IRR.

Instructions for Understanding Table 3.

- The **1st** column of Table 3 lists medical problems that were commonly reported during Part 4 of the study. All medical problems reported by more than 10% of participants are listed.
- The **2nd** and **3rd** columns tell how many of the 3 participants receiving ontorpacept 0.5 mg/kg and ontorpacept 0.7 mg/kg reported each medical problem. Next to this number is the percentage of the 3 participants receiving ontorpacept 0.5 mg/kg and 0.7 mg/kg who reported the medical problem.
- The **4th** column tells how many of the 6 participants receiving ontorpacept 1.0 mg/kg reported each medical problem. Next to this number is the percentage of the 6 participants receiving ontorpacept 1.0 mg/kg who reported the medical problem.
- The **5th** column tells how many of the 3 participants receiving ontorpacept 1.4 mg/kg reported each medical problem. Next to this number is the percentage of the 3 participants receiving ontorpacept 1.4 mg/kg who reported the medical problem.
- The **6th** column tells how many of the 12 participants receiving ontorpacept 2.0 mg/kg reported each medical problem. Next to this number is the percentage of the 12 participants receiving ontorpacept 2.0 mg/kg who reported the medical problem.
- The **7th** column tells how many of the 4 participants receiving ontorpacept Q2W 2.0 mg/kg reported each medical problem.

Next to this number is the percentage of the 4 participants receiving ontorpacept Q2W 2.0 mg/kg who reported the medical problem.

- Using these instructions, you can see that 1 out of the 3 (33.3%) participants receiving ontorpacept 0.5 mg/kg, 2 out of the 3 (66.7%) participants receiving ontorpacept 0.7 mg/kg, 5 out of the 6 (83.3%) participants receiving ontorpacept 1.0 mg/kg, 2 out of the 3 (66.7%) participants receiving ontorpacept 1.4 mg/kg, 5 out of the 12 (41.7%) participants receiving ontorpacept 2.0 mg/kg, and all 4 (100.0%) participants receiving ontorpacept Q2W 2.0 mg/kg reported IRR.

Table 1. Commonly reported medical problems reported for more than 10% of study participants in Part 1

Medical Problem	Ontorpacept 0.05 mg/kg (3 Participants)	Ontorpacept 0.1 mg/kg (3 Participants)	Ontorpacept 0.2 mg/kg (7 Participants)	Ontorpacept 0.3 mg/kg (5 Participants)
IRR	2 out of 3 participants (66.7%)	2 out of 3 participants (66.7%)	4 out of 7 participants (57.1%)	4 out of 5 participants (80.0%)
Feeling tired	1 out of 3 participants (33.3%)	2 out of 3 participants (66.7%)	4 out of 7 participants (57.1%)	2 out of 5 participants (40.0%)

Table 1. Commonly reported medical problems reported for more than 10% of study participants in Part 1

Medical Problem	Ontorpacept 0.05 mg/kg (3 Participants)	Ontorpacept 0.1 mg/kg (3 Participants)	Ontorpacept 0.2 mg/kg (7 Participants)	Ontorpacept 0.3 mg/kg (5 Participants)
Chills	0 out of 3 participants (0%)	0 out of 3 participants (0%)	2 out of 7 participants (28.6%)	0 out of 5 participants (0%)
Low red blood cells	0 out of 3 participants (0%)	0 out of 3 participants (0%)	0 out of 7 participants (0%)	1 out of 5 participants (20.0%)
Fever	0 out of 3 participants (0%)	0 out of 3 participants (0%)	0 out of 7 participants (0%)	1 out of 5 participants (20.0%)
Platelet level decreased	0 out of 3 participants (0%)	0 out of 3 participants (0%)	0 out of 7 participants (0%)	2 out of 5 participants (40.0%)
Upset stomach	0 out of 3 participants (0%)	1 out of 3 participants (33.3%)	0 out of 7 participants (0%)	2 out of 5 participants (40.0%)
Diarrhea (loose stools)	2 out of 3 participants (66.7%)	0 out of 3 participants (0%)	4 out of 7 participants (57.1%)	3 out of 5 participants (60.0%)

Table 1. Commonly reported medical problems reported for more than 10% of study participants in Part 1

Medical Problem	Ontorpacept 0.05 mg/kg (3 Participants)	Ontorpacept 0.1 mg/kg (3 Participants)	Ontorpacept 0.2 mg/kg (7 Participants)	Ontorpacept 0.3 mg/kg (5 Participants)
Low levels of platelets	0 out of 3 participants (0%)	0 out of 3 participants (0%)	1 out of 7 participants (14.3%)	2 out of 5 participants (40.0%)
Headache	0 out of 3 participants (0%)	1 out of 3 participants (33.3%)	3 out of 7 participants (42.9%)	0 out of 5 participants (0%)
Difficulty breathing	0 out of 3 participants (0%)	0 out of 3 participants (0%)	2 out of 7 participants (28.6%)	0 out of 5 participants (0%)
Itching	0 out of 3 participants (0%)	2 out of 3 participants (66.7%)	0 out of 7 participants (0%)	0 out of 5 participants (0%)
Vomiting	0 out of 3 participants (0%)	1 out of 3 participants (33.3%)	0 out of 7 participants (0%)	1 out of 5 participants (20.0%)
Cough	1 out of 3 participants (33.3%)	1 out of 3 participants (33.3%)	1 out of 7 participants (14.3%)	0 out of 5 participants (0%)

Table 1. Commonly reported medical problems reported for more than 10% of study participants in Part 1				
Medical Problem	**Ontorpacept 0.05 mg/kg (3 Participants)**	**Ontorpacept 0.1 mg/kg (3 Participants)**	**Ontorpacept 0.2 mg/kg (7 Participants)**	**Ontorpacept 0.3 mg/kg (5 Participants)**
Joint pain	1 out of 3 participants (33.3%)	0 out of 3 participants (0%)	1 out of 7 participants (14.3%)	1 out of 5 participants (20.0%)
Dizziness	0 out of 3 participants (0%)	0 out of 3 participants (0%)	0 out of 7 participants (0%)	1 out of 5 participants (20.0%)
Not feeling hungry	0 out of 3 participants (0%)	0 out of 3 participants (0%)	0 out of 7 participants (0%)	1 out of 5 participants (20.0%)
Constipation	0 out of 3 participants (0%)	0 out of 3 participants (0%)	1 out of 7 participants (14.3%)	2 out of 5 participants (40.0%)

Table 2. Commonly reported medical problems reported for more than 10% of study participants in Part 2 and Part 3

Medical Problem	Part 2 Ontorpacept Monotherapy (107 Participants)	Part 3 Ontorpacept Monotherapy (42 Participants)	Part 2 Nivolumab Combination (11 Participants)	Part 2 Rituximab Combination (40 Participants)
IRR	46 out of 107 participants (43.0%)	16 out of 42 participants (38.1%)	5 out of 11 participants (45.5%)	17 out of 40 participants (42.5%)
Feeling tired	39 out of 107 participants (36.4%)	13 out of 42 participants (31.0%)	0 out of 11 participants (0%)	18 out of 40 participants (45.0%)
Chills	28 out of 107 participants (26.2%)	16 out of 42 participants (38.1%)	5 out of 11 participants (45.5%)	5 out of 40 participants (12.5%)
Low red blood cells	31 out of 107 participants (29.0%)	8 out of 42 participants (19.0%)	4 out of 11 participants (36.4%)	10 out of 40 participants (25.0%)
Fever	25 out of 107 participants (23.4%)	10 out of 42 participants (23.8%)	4 out of 11 participants (36.4%)	10 out of 40 participants (25.0%)
Platelet level in blood decreased	20 out of 107 participants (18.7%)	10 out of 42 participants (23.8%)	3 out of 11 participants (27.3%)	7 out of 40 participants (17.5%)

Table 2. Commonly reported medical problems reported for more than 10% of study participants in Part 2 and Part 3

Medical Problem	Part 2 Ontorpacept Monotherapy (107 Participants)	Part 3 Ontorpacept Monotherapy (42 Participants)	Part 2 Nivolumab Combination (11 Participants)	Part 2 Rituximab Combination (40 Participants)
Upset stomach	28 out of 107 participants (26.2%)	6 out of 42 participants (14.3%)	3 out of 11 participants (27.3%)	8 out of 40 participants (20.0%)
Diarrhea (loose stools)	23 out of 107 participants (21.5%)	5 out of 42 participants (11.9%)	2 out of 11 participants (18.2%)	8 out of 40 participants (20.0%)
Low levels of platelets	24 out of 107 participants (22.4%)	6 out of 42 participants (14.3%)	3 out of 11 participants (27.3%)	6 out of 40 participants (15.0%)
Headache	20 out of 107 participants (18.7%)	5 out of 42 participants (11.9%)	4 out of 11 participants (36.4%)	4 out of 40 participants (10.0%)
Difficulty breathing	17 out of 107 participants (15.9%)	9 out of 42 participants (21.4%)	1 out of 11 participants (9.1%)	3 out of 40 participants (7.5%)
Itching	11 out of 107 participants (10.3%)	8 out of 42 participants (19.0%)	1 out of 11 participants (9.1%)	4 out of 40 participants (10.0%)

Table 2. Commonly reported medical problems reported for more than 10% of study participants in Part 2 and Part 3

Medical Problem	Part 2 Ontorpacept Monotherapy (107 Participants)	Part 3 Ontorpacept Monotherapy (42 Participants)	Part 2 Nivolumab Combination (11 Participants)	Part 2 Rituximab Combination (40 Participants)
Vomiting	20 out of 107 participants (18.7%)	1 out of 42 participants (2.4%)	2 out of 11 participants (18.2%)	7 out of 40 participants (17.5%)
Cough	14 out of 107 participants (13.1%)	6 out of 42 participants (14.3%)	0 out of 11 participants (0%)	8 out of 40 participants (20.0%)
Joint pain	12 out of 107 participants (11.2%)	5 out of 42 participants (11.9%)	1 out of 11 participants (9.1%)	9 out of 40 participants (22.5%)
Dizziness	16 out of 107 participants (15.0%)	6 out of 42 participants (14.3%)	0 out of 11 participants (0%)	3 out of 40 participants (7.5%)
Not feeling hungry	15 out of 107 participants (14.0%)	4 out of 42 participants (9.5%)	0 out of 11 participants (0%)	5 out of 40 participants (12.5%)
Constipation	11 out of 107 participants (10.3%)	2 out of 42 participants (4.8%)	3 out of 11 participants (27.3%)	6 out of 40 participants (15.0%)

Table 3. Commonly reported medical problems reported for more than 10% of study participants in Part 4

	Dose levels of Ontorpacept in Part 4					
Medical Problem	**0.5 mg/kg (3 participants)**	**0.7 mg/kg (3 participants)**	**1.0 mg/kg (6 participants)**	**1.4 mg/kg (3 participants**	**2.0 mg/kg (12 participants)**	**Q2W 2.0 mg/kg (4 participants)**
IRR	1 out of 3 participants (33.3%)	2 out of 3 participants (66.7%)	5 out of 6 participants (83.3%)	2 out of 3 participants (66.7%)	5 out of 12 participants (41.7%)	4 out of 4 participants (100.0%)
Feeling tired	1 out of 3 participants (33.3%)	0 out of 3 participants (0%)	1 out of 6 participants (16.7%)	0 out of 3 participants (0%)	4 out of 12 participants (33.3%)	0 out of 4 participants (0%)
Chills	0 out of 3 participants (0%)	0 out of 3 participants (0%)	2 out of 6 participants (33.3%)	0 out of 3 participants (0%)	0 out of 12 participants (0%)	1 out of 4 participants (25.0%)
Low red blood cells	0 out of 3 participants (0%)	0 out of 3 participants (0%)	0 out of 6 participants (0%)	0 out of 3 participants (0%)	2 out of 12 participants (16.7%)	2 out of 4 participants (50.0%)
Fever	1 out of 3 participants (33.3%)	1 out of 3 participants (33.3%)	2 out of 6 participants (33.3%)	0 out of 3 participants (0%)	2 out of 12 participants (16.7%)	1 out of 4 participants (25.0%)
Platelet level decreased	0 out of 3 participants (0%)	0 out of 3 participants (0%)	1 out of 6 participants (16.7%)	1 out of 3 participants (33.3%)	8 out of 12 participants (66.7%)	1 out of 4 participants (25.0%)

Table 3. Commonly reported medical problems reported for more than 10% of study participants in Part 4

	Dose levels of Ontorpacept in Part 4					
Medical Problem	**0.5 mg/kg (3 participants)**	**0.7 mg/kg (3 participants)**	**1.0 mg/kg (6 participants)**	**1.4 mg/kg (3 participants**	**2.0 mg/kg (12 participants)**	**Q2W 2.0 mg/kg (4 participants)**
Upset stomach	0 out of 3 participants (0%)	1 out of 3 participants (33.3%)	1 out of 6 participants (16.7%)	1 out of 3 participants (33.3%)	1 out of 12 participants (8.3%)	0 out of 4 participants (0%)
Diarrhea (loose stools)	0 out of 3 participants (0%)	1 out of 3 participants (33.3%)	2 out of 6 participants (33.3%)	0 out of 3 participants (0%)	1 out of 12 participants (8.3%)	0 out of 4 participants (0%)
Low levels of platelets	0 out of 3 participants (0%)	1 out of 3 participants (33.3%)	0 out of 6 participants (0%)	0 out of 3 participants (0%)	2 out of 12 participants (16.7%)	1 out of 4 participants (25.0%)
Headache	0 out of 3 participants (0%)	0 out of 3 participants (0%)	2 out of 6 participants (33.3%)	2 out of 3 participants (66.7%)	2 out of 12 participants (16.7%)	0 out of 4 participants (0%)
Difficulty breathing	1 out of 3 participants (33.3%)	0 out of 3 participants (0%)	1 out of 6 participants (16.7%)	1 out of 3 participants (33.3%)	2 out of 12 participants (16.7%)	1 out of 4 participants (25.0%)
Itching	1 out of 3 participants (33.3%)	2 out of 3 participants (66.7%)	2 out of 6 participants (33.3%)	1 out of 3 participants (33.3%)	2 out of 12 participants (16.7%)	0 out of 4 participants (0%)

Table 3. Commonly reported medical problems reported for more than 10% of study participants in Part 4

	Dose levels of Ontorpacept in Part 4					
Medical Problem	**0.5 mg/kg (3 participants)**	**0.7 mg/kg (3 participants)**	**1.0 mg/kg (6 participants)**	**1.4 mg/kg (3 participants**	**2.0 mg/kg (12 participants)**	**Q2W 2.0 mg/kg (4 participants)**
Vomiting	0 out of 3 participants (0%)	1 out of 3 participants (33.3%)	0 out of 6 participants (0%)	1 out of 3 participants (33.3%)	0 out of 12 participants (0%)	0 out of 4 participants (0%)
Cough	1 out of 3 participants (33.3%)	0 out of 3 participants (0%)	0 out of 6 participants (0%)	0 out of 3 participants (0%)	1 out of 12 participants (8.3%)	0 out of 4 participants (0%)
Joint pain	0 out of 3 participants (0%)	0 out of 3 participants (0%)	0 out of 6 participants (0%)	1 out of 3 participants (33.3%)	0 out of 12 participants (0%)	0 out of 4 participants (0%)
Dizziness	0 out of 3 participants (0%)	0 out of 3 participants (0%)	0 out of 6 participants (0%)	1 out of 3 participants (33.3%)	2 out of 12 participants (16.7%)	0 out of 4 participants (0%)
Not feeling hungry	0 out of 3 participants (0%)	0 out of 3 participants (0%)	1 out of 6 participants (16.7%)	0 out of 3 participants (0%)	0 out of 12 participants (0%)	0 out of 4 participants (0%)
Low levels of white blood cells	0 out of 3 participants (0%)	0 out of 3 participants (0%)	0 out of 6 participants (0%)	1 out of 3 participants (33.3%)	3 out of 12 participants (25.0%)	0 out of 4 participants (0%)

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.

Part 1 and Part 4

In the dose levels of 0.3 mg/kg for Parts 1 and 2 mg/kg and Q2W 2.0 mg/kg in Part 4, at least 1 participant had multiple treatment-emergent serious medical problems.

- Part 1 of the study included these events:
  - IRR (1 participant at 0.05 mg/kg dose), difficulty in breathing (1 participant at 0.2 mg/kg dose), stomach flu, low levels of platelets and low blood levels of potassium (1 participant each at 0.3 mg/kg dose).
  - Three (16.7%) participants in Part 1 died in the study. Of which 2 (11.1%) participants died due to disease under study.
- Part 4 of the study included these events:
  - Skin infection (1 participant at 0.5 mg/kg dose), major depression (1 participant at 0.7 mg/kg dose), IRR and stroke (1 participant each at 1.0 mg/kg dose), bacterial infection leading to peptic ulcer (ulcers in the stomach), Covid-19 pneumonia (infection of the lungs), viral infection, and loss of consciousness (1 participant each at 2.0 mg/kg dose), pneumonia aspiration (a type of infection of the lungs), fracture in the hip, inflammation of the stomach lining and fever (1 participant each at Q2W 2.0 mg/kg dose).

- Eight (25.8%) participants in Part 4 died in the study. Of which 4 (12.9%) participants died due to disease under study.

Parts 2 and 3

- In Part 2, a total of 43 out of 107 (40.2%) participants who received ontorpacept monotherapy, 2 out of 11 (18.2%) participants who received nivolumab combination and 13 out of 40 (32.5%) participants who received rituximab combination had serious treatment-emergent medical problems.
- In Part 3, 15 out of 42 (35.7%) participants who received ontorpacept monotherapy had serious treatment-emergent medical problems. The most common serious medical problems – those reported by more than 3% of participants in Parts 2 and 3 – are described in Table 4.

Below are instructions on how to read Table 4.

Instructions for Understanding Table 4

- The **1st** column of Table 4 lists serious medical problems that were commonly reported during Part 2 and Part 3 of the study. All medical problems reported by more than 3% of participants are listed.
- The **2nd** column tells how many of the 107 participants receiving ontorpacept monotherapy in Part 2 reported each medical problem. Next to this number is the percentage of the 107 participants receiving ontorpacept monotherapy who reported the medical problem.
- The **3rd** column tells how many of the 42 participants receiving ontorpacept monotherapy in Part 3 reported each medical problem. Next to this number is the percentage of the

42 participants receiving ontorpacept monotherapy who reported the medical problem.

- The **4th** column tells how many of the 11 participants receiving ontorpacept together with nivolumab in Part 2 reported each medical problem. Next to this number is the percentage of the 11 participants receiving ontorpacept together with nivolumab who reported the medical problem.
- The **5th** column tells how many of the 40 participants receiving ontorpacept together with rituximab in Part 2 reported each medical problem. Next to this number is the percentage of the 40 participants receiving ontorpacept together with rituximab who reported the medical problem.
- Using these instructions, you can see that 4 out of 107 participants (3.7%) participants receiving ontorpacept monotherapy in Part 2 of the study, 3 out of 42 participants (7.1%) receiving ontorpacept monotherapy in Part 3 of the study, and 1 out of 40 participants (2.5%) receiving ontorpacept in combination with rituximab reported serious infection.

- In Part 2, 52 (48.6%) participants in ontorpacept monotherapy cohort and 16 (38.1%) participants in Part 3 ontorpacept monotherapy cohort died in the study.
- The most common reason for death was disease under study: 37 (34.6%) participants in Part 2 ontorpacept monotherapy cohort, and 10 (23.8%) participants in Part 3 ontorpacept monotherapy cohort died due to disease under study.

Table 4. Commonly reported serious medical problems reported for more than 3% of study participants in Part 2 and Part 3

Serious Medical Problem	Part 2 Ontorpacept Monotherapy (107 Participants)	Part 3 Ontorpacept Monotherapy (42 Participants)	Part 2 Nivolumab Combination (11 Participants)	Part 2 Rituximab Combination (40 Participants)
Serious infection	4 out of 107 participants (3.7%)	3 out of 42 participants (7.1%)	0 out of 11 participants (0%)	1 out of 40 participants (2.5%)
Lung infection	3 out of 107 participants (2.8%)	2 out of 42 participants (4.8%)	0 out of 11 participants (0%)	1 out of 40 participants (2.5%)
Infection of the blood	4 out of 107 participants (3.7%)	0 out of 42 participants (0%)	0 out of 11 participants (0%)	1 out of 40 participants (2.5%)
Inflammation of the deep skin tissue	0 out of 107 participants (0%)	1 out of 42 participants (2.4%)	0 out of 11 participants (0%)	2 out of 40 participants (5.0%)
IRR	3 out of 107 participants (2.8%)	2 out of 42 participants (4.8%)	0 out of 11 participants (0%)	0 out of 40 participants (0%)

Table 4. Commonly reported serious medical problems reported for more than 3% of study participants in Part 2 and Part 3

Serious Medical Problem	Part 2 Ontorpacept Monotherapy (107 Participants)	Part 3 Ontorpacept Monotherapy (42 Participants)	Part 2 Nivolumab Combination (11 Participants)	Part 2 Rituximab Combination (40 Participants)
Bleeding in stomach and gut	0 out of 107 participants (0%)	0 out of 42 participants (0%)	0 out of 11 participants (0%)	2 out of 40 participants (5.0%)
Sores in mouth	0 out of 107 participants (0%)	0 out of 42 participants (0%)	1 out of 11 participants (9.1%)	0 out of 40 participants (0%)
Fever	2 out of 107 participants (1.9%)	0 out of 42 participants (0%)	1 out of 11 participants (9.1%)	0 out of 40 participants (0%)
Dehydration	0 out of 107 participants (0%)	0 out of 42 participants (0%)	1 out of 11 participants (9.1%)	1 out of 40 participants (2.5%)
Lung inflammation	0 out of 107 participants (0%)	0 out of 42 participants (0%)	1 out of 11 participants (9.1%)	0 out of 40 participants (0%)
Platelet level decreased	0 out of 107 participants (0%)	0 out of 42 participants (0%)	1 out of 11 participants (9.1%)	0 out of 40 participants (0%)

Table 4. Commonly reported serious medical problems reported for more than 3% of study participants in Part 2 and Part 3				
Serious Medical Problem	**Part 2 Ontorpacept Monotherapy (107 Participants)**	**Part 3 Ontorpacept Monotherapy (42 Participants)**	**Part 2 Nivolumab Combination (11 Participants)**	**Part 2 Rituximab Combination (40 Participants)**
Sudden injury in the kidney	0 out of 107 participants (0%)	2 out of 42 participants (4.8%)	0 out of 11 participants (0%)	0 out of 40 participants (0%)

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 C4961001

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

www.clinicaltrials.gov	Use the study identifier **NCT02663518**

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!