CLINICAL TRIAL 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 medicine 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: ARRY-382 (PF-07265804)

Protocol Number: ARRAY-382-201 (C4261001)

Dates of Trial: 01 September 2016 to 24 October 2019

Title of this Trial: A Study of ARRY-382 in Combination With Pembrolizumab for the Treatment of Patients With Advanced Solid Tumors

[A Phase 1b/2 Study of ARRY-382 in Combination with Pembrolizumab, a Programmed Cell Death Receptor 1 (PD-1) Antibody, for the Treatment of Patients with Advanced Solid Tumors]

Date(s) of this Report: 26 October 2020

– Thank You –

Pfizer, the Sponsor, would like to thank you for your participation in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results, please contact the doctor or staff at your study site.

WHY WAS THIS STUDY DONE?

Many treatments for cancer work by trying to help the body's immune system attack and kill cancer cells. However, these treatments do not work for all patients, and some only work for a short time before the patient's cancer gets worse. Researchers think that combining different medications that help the immune system fight cancer in different ways could help patients' cancer get better.

ARRY-382 is a study drug that has not been approved by the United States Food and Drug Administration (FDA). ARRY-382 is taken by mouth once a day. ARRY-382 is thought to work by helping the immune system slow or stop the growth of cancer cells. Pembrolizumab is approved by the FDA for the treatment of patients with many different types of cancer, and is given through a needle into a vein (IV). Pembrolizumab also works by helping the immune system slow or stop the growth of cancer cells, but in a different way than ARRY-382. Studies in animals found that combining these 2 types of medicines helped the immune system do a better job of slowing the growth of tumors.

This study was divided into 2 parts, or "phases". The main purpose of the first phase of the study (Phase 1) was to determine the best dose of ARRY-382 to use in Phase 2 when given with the drug pembrolizumab. To do this, the researchers asked,

- **What dose-limiting toxicities, or "DLTs", did patients have when taking ARRY-382 with pembrolizumab?**

  DLTs are certain medical problems caused by taking ARRY-382 with pembrolizumab which require the patient to lower the dose or stop taking the medicine temporarily or permanently.

Phase 2 of the study was designed to see whether ARRY-382, when taken together with the drug pembrolizumab, had a beneficial effect on the patients' cancer (improved symptoms, reduced rate of tumor growth or decreased the size of tumors in the body). To do this, the researchers asked,

- **How many patients had their cancer get better when taking ARRY-382 with pembrolizumab?**

The researchers also monitored the patients for any medical problems that they had during the study.

WHAT HAPPENED DURING THE STUDY?

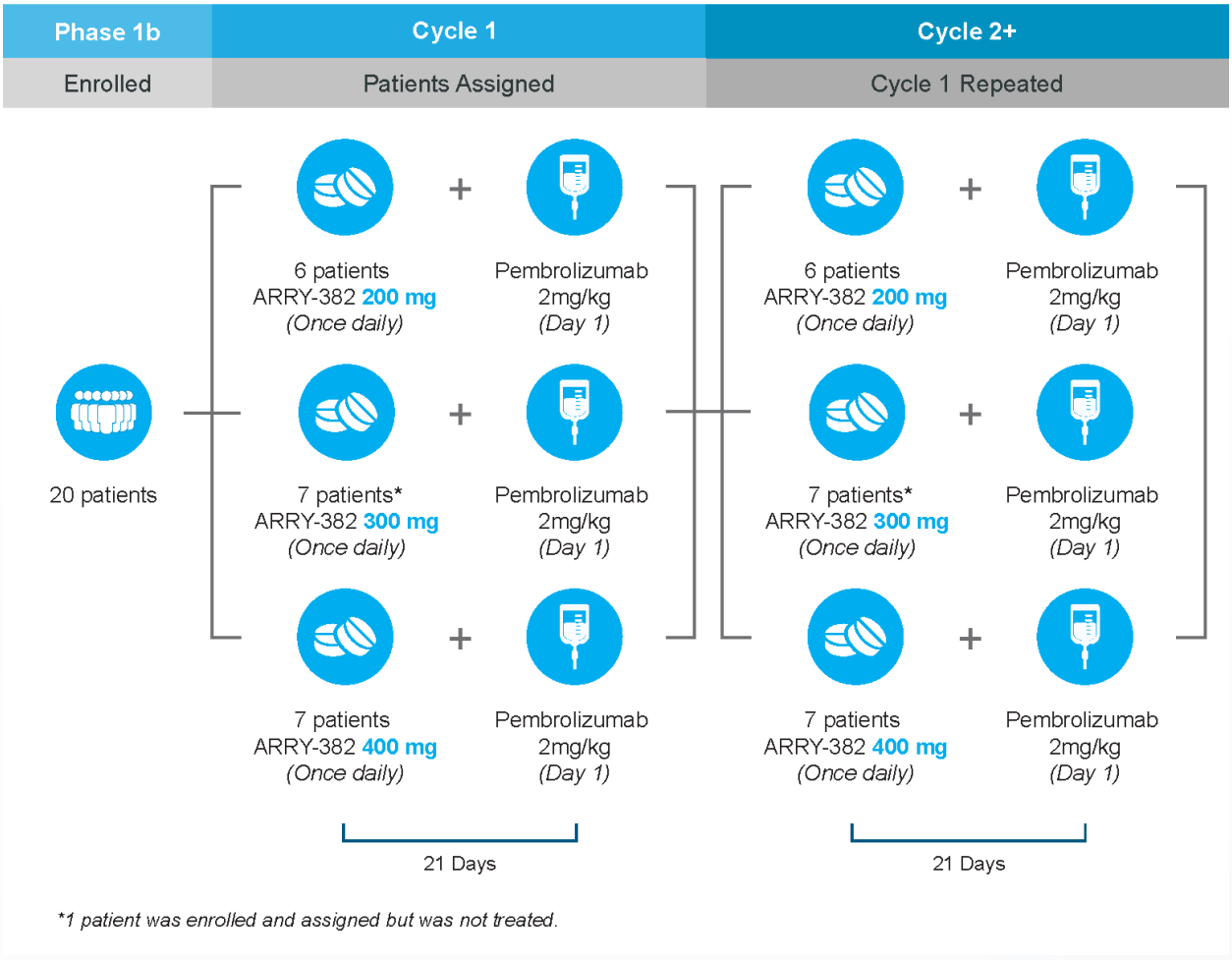
This study included patients who met the following conditions:

- Aged 18 years or older
- For Phase 1:
  - Diagnosed with one of certain types of cancer, such as of the ovaries, breast, head and neck, bladder, colon, pancreas, stomach, skin, or lung
  - Cancer had not responded to standard treatment, was not currently treatable, or the patient had refused standard treatment
- For Phase 2:
  - Advanced solid tumor cancer that had gotten worse while being treated with certain types of anti-cancer therapy (called "PD-1/PD-L1 inhibitor resistant")
  - Advanced cancer of the ovaries, abdomen (peritoneum), or fallopian tubes that got worse within 6 months of being treated with ≥ 4 cycles of platinum-based chemotherapy (called "platinum-resistant")
  - Advanced pancreatic cancer (PDS) that had been treated at least once before
- Able to walk around, take care of themselves, and do light house work or office work
- Had adequate kidney, liver, bone marrow, and heart function
- Had not been treated before with cancer medications called 'checkpoint inhibitors' (such as a PD-1, PD-L1, or CTLA-4 inhibitor)

This was an "open-label" study, which means that the patients and doctors knew what dose of ARRY-382 and pembrolizumab the patients were receiving.

What happened during Phase 1 of the study?

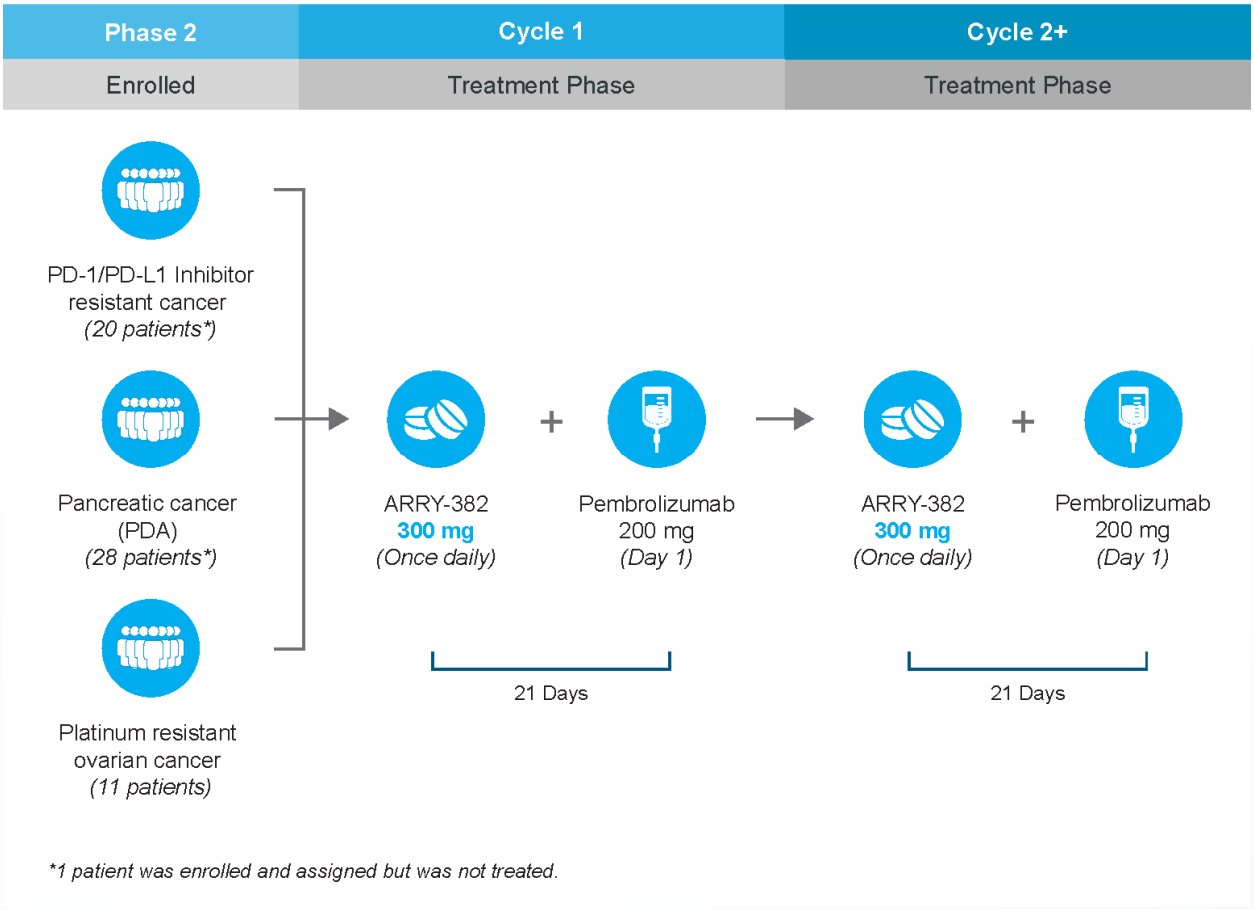
Phase 1 of this study compared 3 groups of patients that were assigned to 1 of 3 doses of ARRY-382 (either 200 mg, 300 mg, or 400 mg per day) to find the recommended dose of ARRY-382 for the Phase 2 portion of the study. The figure below shows what happened during Phase 1 of the study.



During Phase 1, each patient took 1 of 3 doses of ARRY-382 in pill form, once daily by mouth for 21 days. The patients were also treated with pembrolizumab IV once every 3 weeks and monitored for medical problems.

What happened during Phase 2 of the study?

Phase 2 of this study compared 3 groups of patients with different types of cancer to see if their cancer got better with ARRY-382 and pembrolizumab treatment. Based on the Phase 1 results, all of the patients in Phase 2 were assigned to take 200 mg ARRY-382 once daily. The figure below shows what happened during Phase 2 of the study.



While many patients were only in the study for a few months, the entire study took just over 3 years to complete. The Sponsor ran this study at 15 locations in the United States of America. It began on 01 September 2016 and ended 24 October 2019. A total of 10 men and 9 women participated in Phase 1 and 22 men and 35 women participated in Phase 2. All patients were between the ages of 30 and 87.

Patients were to be treated until their cancer stopped responding or got worse, until they developed unacceptable medical problems, or until they chose to stop treatment. All patients who started Phase 1 or Phase 2 of the study stopped taking the study medicines before the study ended. Most patients left before the study was over because their cancer had gotten worse, by their choice, or because a doctor decided it was best for a patient to stop being in the study.

This study was stopped when early results showed that too few patients had their cancer get better when taking ARRY-382 and pembrolizumab. When the study ended in October 2019, the Sponsor reviewed 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?

During Phase 1 of the study, what dose-limiting toxicities (DLT) were reported when taking ARRY-382 with pembrolizumab?

During Phase 1, researchers wanted to find the correct dose of ARRY-382 for treating patients with cancer when taken with pembrolizumab. To find the correct dose, the researchers needed to know how many patients in each dose group had a DLT during their first 21-day treatment cycle.

There were 2 patients who took 400 mg ARRY-382 and 1 patient who took 300 mg ARRY-382 who had DLT. Of the 3 patients, 1 had increased muscle enzyme levels in their blood (CPK), 1 had increased liver enzymes in their blood (ALT/AST and bilirubin), and 1 had acute pancreatitis. Some of the other patients who took 200 mg, 300 mg, or 400 mg of ARRY-382 once a day had other medical problems that caused them to temporarily stop or lower their dose of ARRY-382. Using this information, the researchers decided that 300 mg once a day was the correct ARRY-382 dose to use with pembrolizumab during Phase 2 of the study.

During Phase 2 of the study, how many patients had their cancer get better when taking ARRY-382 with pembrolizumab?

One (1) patient out of 27 (4%) with pancreatic cancer (PDA) had their cancer get better while taking ARRY-382 with pembrolizumab. None of the patients with "PD-1/PD-L1 inhibitor resistant" cancer or "platinum-resistant" ovarian cancer had their cancer get better. The percentage of patients whose cancer stayed the same was 42% for PD-1/PD-L1 refractory cancer, 19% for pancreatic cancer (PDA), and 36% for platinum-resistant ovarian cancer. These results did not show that one treatment was better than another. The differences seen could have been due to chance.

This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

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 the side effects of an experimental drug might be.

Eighteen (18) out of 19 patients in Phase 1 of this study had at least 1 medical problem. Two (2) patients in Phase 1 left the study because of medical problems. Fifty-six (56) of 57 patients in Phase 2 of this study had at least 1 medical problem. A total of 10 patients in Phase 2 left the study because of medical problems. The most common medical problems in Phase 1 and Phase 2 are listed below and on the next 2 pages.

Most Common Medical Problems in Phase 1 (Reported by 20% or More of Patients)

Medical Problem	Pembrolizumab 2 mg/kg		
	ARRY-382 200 mg (6 Patients Treated)	ARRY-382 400 mg (7 Patients Treated)	ARRY-382 300 mg (6 Patients Treated)
Increased liver enzyme in blood (AST)	2 (33%)	4 (57%)	6 (100%)
Increased muscle enzyme in blood (CPK)	2 (33%)	3 (43%)	3 (50%)

Increased liver enzyme in blood (ALT)	2 (33%)	2 (29%)	3 (50%)
Tiredness	2 (33%)	3 (43%)	2 (33%)
Fever	2 (33%)	3 (43%)	2 (33%)
Increased liver enzyme in blood (alkaline phosphatase)	1 (17%)	3 (43%)	2 (33%)
Increased digestive enzyme in blood (Lipase)	1 (17%)	1 (14%)	4 (67%)
Increased digestive enzyme in blood (Amylase)	1 (17%)	1 (14%)	3 (50%)
Low red blood cells (anemia)	1 (17%)	4 (57%)	0
Nausea	1 (17%)	3 (43%)	1 (17%)
Itching skin	2 (33%)	0	2 (33%)
Flat red skin rash	1 (17%)	1 (14%)	2 (33%)
Vomiting	1 (17%)	1 (14%)	2 (33%)

Most Common Medical Problems in Phase 2 (Reported by 15% or More of Patients)

	Pembrolizumab 200 mg + ARRY-382 300 mg		
Medical Problem	PD-1/PD-L1 Inhibitor Resistant Cancer (19 Patients Treated)	Pancreatic Cancer (27 Patients Treated)	Platinum-Resistant Ovarian Cancer (11 Patients Treated)
Tiredness	10 (53%)	16 (59%)	3 (27%)
Nausea	9 (47%)	13 (48%)	5 (46%)
Increased liver enzyme in blood (AST)	8 (42%)	9 (33%)	4 (36%)

Vomiting	**8 (42%)**	**9 (33%)**	**1 (9%)**
Increased muscle enzyme in blood (CPK)	**9 (47%)**	**5 (19%)**	**2 (18%)**
Abdominal pain	**4 (21%)**	**7 (26%)**	**4 (36%)**
Low red blood cells (anemia)	**5 (26%)**	**9 (33%)**	**1 (9%)**
Low appetite	**3 (16%)**	**9 (33%)**	**2 (18%)**
Diarrhea	**8 (42%)**	**4 (15%)**	**2 (18%)**
Increased liver enzyme in blood (ALT)	**3 (16%)**	**5 (19%)**	**4 (36%)**
Constipation	**2 (11%)**	**7 (26%)**	**3 (27%)**
Dehydration	**5 (26%)**	**5 (19%)**	**2 (18%)**
Increased liver enzyme in blood (alkaline phosphatase)	**5(26%)**	**4 (15%)**	**0**
Low blood potassium	**4 (21%)**	**4 (15%)**	**1 (9%)**

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems. A total of 7 patients in Phase 1 (37%, or 7 out of 19 patients) had serious medical problems. A total of 28 patients in Phase 2 (49%, or 28 out of 57 patients) had serious medical problems. Most were not thought to be related to ARRY-382 treatment. Fifteen (15) patients in Phase 1 and 35 patients in Phase 2 passed away during the study. Most deaths were due to the patients' cancer getting worse. The most common serious medical problems in Phase 1 and Phase 2 are shown in the table on the next page.

Serious Medical Problems in Phase 1 (Reported by More Than 1 Patient)

Serious Medical Problem	Pembrolizumab 2 mg/kg		
	ARRY-382 200 mg (6 Patients Treated)	ARRY-382 400 mg (7 Patients Treated)	ARRY-382 300 mg (6 Patients Treated)
Low red blood cells (anemia)	1 (17%)	1 (14%)	0
Lung inflammation	1 (17%)	1 (14%)	0
Fever	0	1 (14%)	1 (17%)

Serious Medical Problems in Phase 2 (Reported by More Than 1 Patient)

Serious Medical Problem	Pembrolizumab 200 mg + ARRY-382 300 mg		
	PD-1/PD-L1 Inhibitor Resistant Cancer (19 Patients Treated)	Pancreatic Cancer (27 Patients Treated)	Platinum-Resistant Ovarian Cancer (11 Patients Treated)
Dehydration	1 (5%)	3 (11%)	0
Buildup of fluid around the lungs	0	2 (7%)	2 (18%)
Abdominal pain	0	1 (4%)	1 (9%)
Low red blood cells (anemia)	1 (5%)	1 (4%)	0
Pneumonia	1 (5%)	0	1 (9%)
Fever	0	2 (7%)	0
Flat red skin rash	1 (5%)	1 (4%)	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. The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT02880371**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **C4261001**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients. No further clinical trials with ARRY-382 are planned at this time.

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