CLINICAL TRIAL RESULTS

This summary reports the results of only one study. Researchers look at the results of many 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: Rivipansel (GMI-1070)

Protocol Number: B5201002 (RESET)

Dates of Trial: 17 June 2015 to 27 June 2019

Title of this Trial: Study Investigating if Treatment with Rivipansel Shortened the Length of Hospital Stay For Patients with Sickle Cell Disease Vaso-Occlusive Crisis

[A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Rivipansel (GMI-1070) in the Treatment of Vaso-Occlusive Crisis in Hospitalized Subjects With Sickle Cell Disease]

Date of this Report: 29 April 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 the results, please contact the doctor or staff at your study site.

WHY WAS THIS STUDY DONE?

Sickle cell disease (SCD) is a common "inherited" blood disorder. Inherited means it is passed down from parents to their children and so runs in families. In the United States, approximately 100,000 people have SCD while around the world it is estimated that at least 5 million people have SCD. A further 100 million people worldwide are thought to carry the SCD trait. This means they may pass SCD to their children, although they do not have any symptoms of SCD themselves. While most people with SCD in the United States are African-American or African, the disease can affect many different ethnic groups including people from the Middle East, India, and the Southern Mediterranean.

Many people with SCD will develop a condition known as an "acute pain crisis" or "vaso-occlusive crisis" (VOC). This happens when cells in the blood of a person with SCD block blood vessels ("vascular occlusion"). This limits blood flow and oxygen delivery to areas of the body ("tissue ischemia"), which causes pain.

Rivipansel is a new type of treatment that was expected to be able to interrupt or lessen the events in the blood vessels that lead to a VOC. The researchers in this study wanted to see if rivipansel treatment could shorten the time that patients had to stay in the hospital for treatment of a VOC.

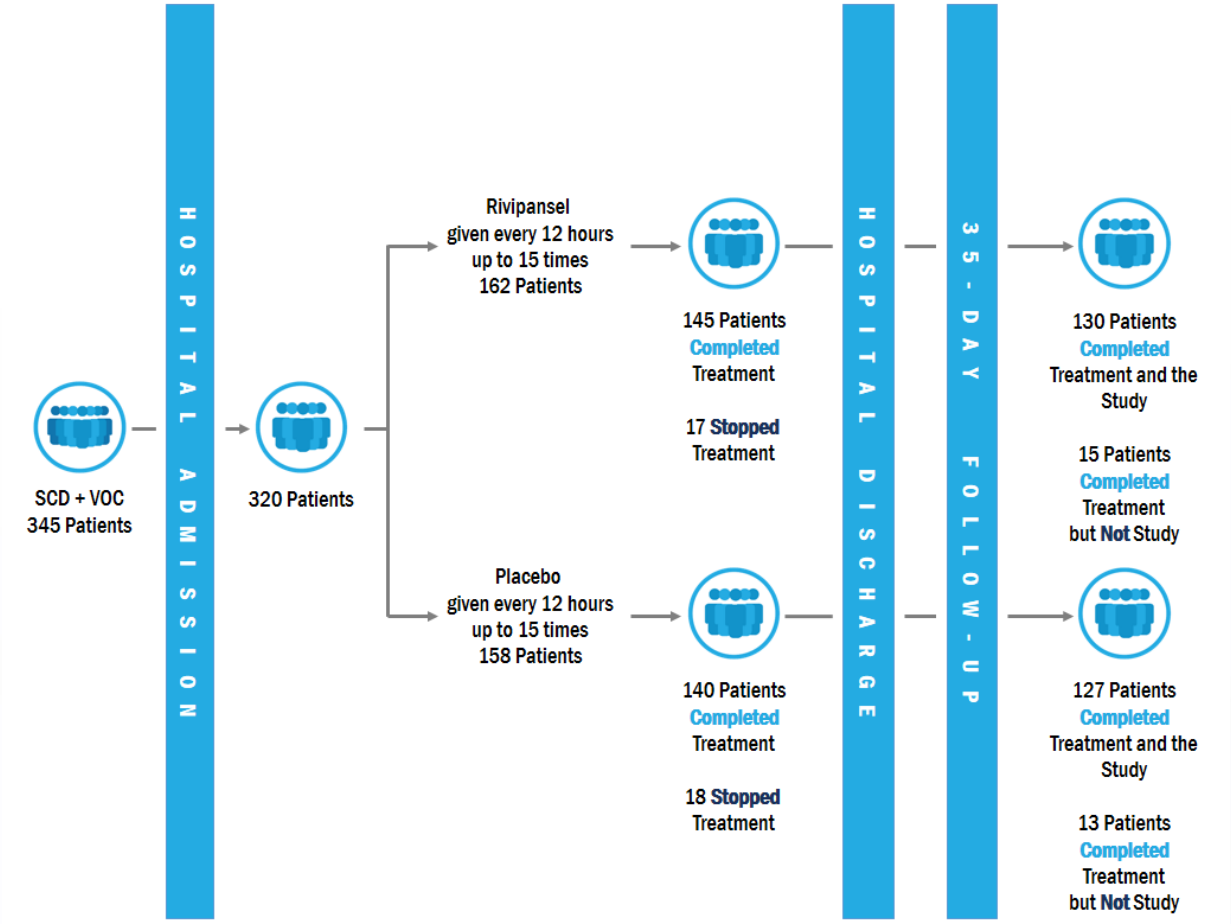
WHAT HAPPENED DURING THE STUDY?

This study compared 2 groups of patients who had SCD to find out if patients given rivipansel spent less time in the hospital before they were ready to be discharged than patients given a "placebo". A placebo does not have any medicine in it but it looks just like the medicine.

The study included patients who were admitted to hospital for treatment of a VOC and needed "intravenous" opioids to provide pain relief. Intravenous means the drug is given into a vein.

The patients and researchers did not know who was given rivipansel and who was given placebo. This is known as a "blinded" study. Patients who opted to join the study were assigned to each group randomly (by chance alone) making this a

"randomized" study. Randomization allows researchers to better compare the 2 treatment groups (rivipansel versus placebo).



SCD: sickle cell disease; VOC: vaso-occlusive crisis.

While individual patients were only in the study for up to 43 days (up to 8 days of treatment with rivipansel or placebo while in the hospital followed by safety assessments for up to 35 days after discharge), the entire study took 4 years to complete. The Sponsor ran this study at 62 locations in the United States and Canada. It began on 17 June 2015 and ended on 27 June 2019. 162 men or boys and 183 women or girls participated. All patients who participated were between the ages of 6 and 59 years.

Patients were to be treated with up to 15 doses of rivipansel or placebo, which was given every 12 hours. Treatment was stopped when a patient was ready to be discharged from the hospital. There were 345 patients who were randomized and started the study and 320 patients who received at least 1 dose of study treatment.

Of these 320 patients, 257 patients completed study treatment and then completed the study - 35 patients discontinued study treatment early, either by their own choice or because a doctor decided it was best for them to stop the study, and 28 patients who completed study treatment did not complete the study.

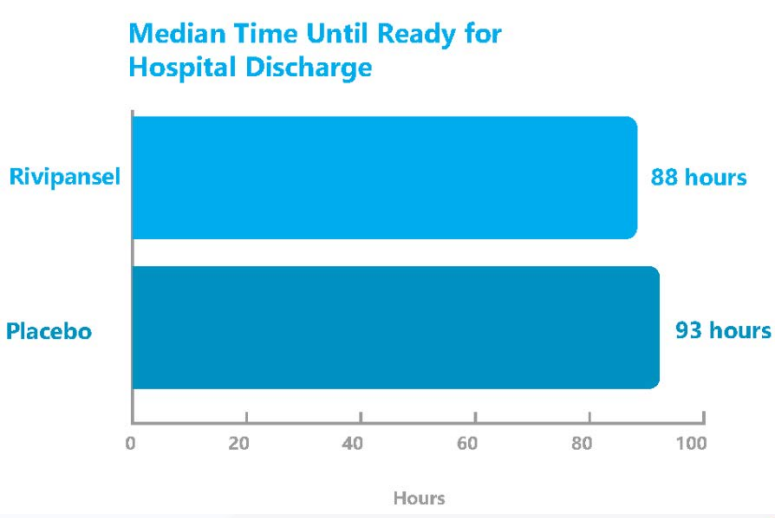
When the study ended in June 2019, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

Were patients who were given rivipansel ready to be discharged from hospital sooner than patients who were given placebo?

The researchers measured, in hours, how long patients stayed in the hospital before they were ready to be discharged and compared the group given rivipansel to the group given placebo. For each group, the number of hours in hospital for each of the patients was recorded and placed in order from the shortest to the longest. The middle number, or "median", for each group was identified to help with the comparison between groups.

Patients in the rivipansel group were in the hospital for a median of 88 hours compared with a median of 93 hours for patients in the placebo group (see figure below).



Based on these data, the study did not show that patients given rivipansel were ready to be discharged any sooner than patients given placebo. The small difference between the 2 groups in the median time until discharge could easily 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 PATIENTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the patients had during the study. Patients could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or occurring by chance) or the medical problem could have been caused by a study treatment or by another medicine the patient was taking. Sometimes the cause of a medical problem can be unknown. By comparing medical problems across treatment groups in many studies, doctors try to understand what the side effects of an experimental drug might be.

273 out of 320 patients in this study reported at least 1 medical problem. Out of the 162 patients who received rivipansel, there was 1 patient who left the study because of a medical problem. None of the 158 patients in the placebo group left the study because of a medical problem. Out of the 320 patients who received rivipansel or placebo in the study, 18 (approximately 6%) had their study treatment stopped because of a medical problem but still continued in the study - 10 out of the 162 patients in the rivipansel group (approximately 6%) and 8 out of the 158 patients in the placebo group (approximately 5%). The most common medical problems that were reported are listed in the following table. Most of these medical problems were considered to be related to the underlying SCD, VOC or treatment (other than rivipansel or placebo) that was given for the VOC.

Most Common Medical Problems (Reported by 5% or More Patients in Either Group)		
Medical Problem	**Rivipansel (162 Patients Treated)**	**Placebo (158 Patients Treated)**
Anemia (low numbers of red blood cells)[a]	18 (11%)	13 (8%)
Hemoglobin decreased[a]	9 (6%)	13 (8%)
Sickle cell anemia with crisis	43 (27%)	47 (30%)
Abdominal pain	9 (6%)	6 (4%)
Constipation (difficulty passing stools)	30 (19%)	21 (13%)
Nausea (feeling like you want to vomit)	26 (16%)	27 (17%)
Vomiting	17 (11%)	16 (10%)
Chest pain	9 (6%)	8 (5%)
Fever or feeling too hot	29 (18%)	33 (21%)
Pain in extremity like arm or leg	9 (6%)	8 (5%)
Feeling dizzy	9 (6%)	4 (3%)
Headache	19 (12%)	30 (19%)
Acute chest syndrome (VOC in lungs)	9 (6%)	10 (6%)
Breathlessness	10 (6%)	3 (2%)
Not getting enough oxygen	9 (6%)	8 (5%)
Itchy skin	24 (15%)	17 (11%)
Rash	9 (6%)	6 (4%)

VOC: vaso-occlusive crisis

[a] In clinical studies, 'anemia' (low numbers of red blood cells) may be reported using different terminology that has the same meaning such as 'hemoglobin decreased'.

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

Out of the 320 patients who received rivipansel or placebo in the study, 101 (approximately 32%) reported serious medical problems. This included 52 out of the 162 patients (approximately 32%) in the rivipansel group and 49 out of the 158 patients (approximately 31%) in the placebo group. The most frequently reported serious medical problems were "sickle cell anemia with crisis" and "acute chest syndrome". Sickle cell anemia with crisis is a term used to describe a VOC and "acute chest syndrome" describes vaso-occlusion when it occurs in the lungs. These serious medical problems were reported in similar numbers of patients in the rivipansel group and the placebo group (see table below). All other serious medical problems were reported in only 1 or 2 patients in either group. None of the patients who were given rivipansel or placebo died during the study.

Most Common Serious Medical Problems (Reported by 5% or More Patients in Either Group)		
Medical Problem	**Rivipansel (162 Patients Treated)**	**Placebo (158 Patients Treated)**
Sickle cell anemia with crisis	**37 (23%)**	**34 (22%)**
Acute chest syndrome (VOC in lungs)	**8 (5%)**	**6 (4%)**

VOC: vaso-occlusive crisis.

WHERE CAN I LEARN MORE ABOUT THIS STUDY?

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

For more details on this study protocol, please visit:

www.clinicaltrials.gov Use the study identifier **NCT02187003**

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

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!