Bling, Delaina A Single Site Retrospective Analysis of the Safety and Efficacy of the Amgen COMMUNITY Study Master of Science (Clinical Research Management) March, 2023, 3 figures, 3 tables, 17 titles

In 2019, a novel respiratory virus surfaced that lead to severe complications in patients and a global pandemic. One of the major issues was COVID-19 associated ARDS. The mortality rate of patients who develop ARDS from a COIVD-19 infection is 45% and at this time there are not many safe and efficacious treatments for the virus. This project exams the Amgen COMMUNITY study at a single site for efficacy and safety. The Amgen study looked at three potential treatments for COVID-19 that would hopefully lessen the occurrence and severity of ARDS; therefore, leading to a lower mortality rate. The efficacy and safety of the Amgen COMMUNITY study was evaluated retrospectively from patients data who participated in the study at the Sunbeam site.

A Single Site Retrospective Analysis of the Safety and Efficacy of the Amgen COMMUNITY Study

Internship Practicum Report

Presented to the Graduate Council of the
School of Biomedical Sciences
University of North Texas
Health Science Center at Fort Worth

In Partial Fulfillment of the Requirements
For the Degree of
MASTER OF SCIENCE IN CLINICAL RESEARCH MANAGEMENT

By Delaina Bling
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CHAPTER I

Introduction/Background

SARS-Cov-2, also known as COVID-19, is a novel coronavirus primarily affecting the respiratory system. First discovered in 2019, infection rates rapidly grew worldwide leading to a pandemic (3). Over the past few years, there have been extensive efforts in the study and treatment of the evolving virus. Unfortunately, one severe side effect of COVID-19 is the development of Acute Respiratory Distress Syndrome (ARDS) in approximately 33% of hospitalized patients (12). ARDS occurs when fluid builds up in the alveoli causing them to become inflamed, ultimately decreasing the oxygen supply to other organs (10). The standard treatment for ARDS is oxygen and ventilation, medication to treat the symptoms, and treating the underlying cause of ARDS (14). Patients with COVID-19 associated ARDS have a mortality rate of 45% and even though there is a standard of treatment for ARDS symptoms via oxygen and ventilation, there are not many efficacious standard treatment options for COVID-19(12).

Given the severity of COVID-19 associated ARDS, the Amgen Covid-19 Multiple Agents and Modulators Unified Industry Members Trial (COMMUNITY) study explored a variety of drugs that would act on different areas of the immune system to block inflammation to reduce and/or prevent the development of ARDS. Three drugs were selected to by studied at the this site: Zilucoplan, Apremilast and Lanadelumab because all three drugs are anti-inflammatory drugs that have been used to treat inflammation in other diseases and could be potentially useful in treating the inflammation associated with COVID-19.

Zilucoplan was chosen as a candidate drug due to its effectiveness at inhibiting the cleavage of complement C5(5). It is an anti-inflammatory peptide that prohibits C5 from cleaving into its two portions: C5a and C5b. This is essential as C5a is known to exacerbate lung injury by binding macrophages and inducing apoptosis of the alveoli(9). Meanwhile, C5b recruits other complements to create the membrane attack complex (MAC) which creates pores in infected cells, allowing for an increased flow of water into the cell which ultimately leads to osmolysis(7). Both of these mechanisms trigger local inflammation in the lungs and can eventually lead to the development of ARDS. Thus, by inhibiting the cleavage of C5, Zilucoplan can aid in the reduction of inflammation in the lungs and the severity of COVID-19 associated ARDS.

Apremilast was chosen due to its effectiveness as a PDE4 inhibitor. Inhibition of PDE4 inhibits the production of TNF-alpha, an inflammatory cytokine(2). The elevation of inflammatory cytokines during infection with COVID-19 is a leading factor in the development of ARDS, a leading cause of death in these patients. Typically, a person produces both inflammatory and anti-inflammatory cytokines during an immune response. When inflammatory cytokines rise, anti-inflammatory cytokines are produced to regulate the amount of inflammation in the body; however, sometimes inflammatory cytokines are no longer regulated by anti-inflammatory cytokines and can lead to the development of a “cytokine storm” which causes severe inflammation. The cytokine storm associated with COVID-19 is primarily caused by TNF-alpha and IL-6; therefore, controlling the cytokine storm could be beneficial in treating COVID-19 and preventing ARDS associated with it(6). Apremilast attempts

to do this by inhibiting the production of TNF-alpha upstream of the pathway via inhibiting the action of PDE4.

Lastly, Lanadelumab was chosen as a candidate drug due to its effectiveness as an IgG monoclonal antibody against plasma kallikrein(pKal). Activation of pKal initiates a cascade that ultimately produces bradykinin, a pro-inflammatory peptide(7). Bradykinin then activates mitogen-activated protein kinases (MAPKs), which in turn upregulate several pro-inflammatory cytokines. An increase in bradykinin, and therefore several pro-inflammatory cytokines, during a COVID-19 infection may be related to several severe symptoms such as ARDS(11). Lanadelumab aims to block the production of these pro-inflammatory cytokines, specifically bradykinin, through the inactivation of pKal.

CHAPTER II

A Single Site Retrospective Analysis of the Safety and Efficacy of the Amgen COMMUNITY Study

Aims

Problem: There is a lack of safe and effective drugs that can be used to treat COVID-19 symptoms.

Aim 1: Analyze patients as being fit-to-discharge based on their ordinal scale rank during the 29-day period

Aim 2: Review the overall safety of the trial

Significance

At the time of this writing in Spring 2023, the threat from COVID-19 seems to have diminished with the development of vaccines; however, this study is still relevant because we continue to see cases daily and at-risk population are continuing to develop severe symptoms. At this time, there are only two drugs that are FDA approved for the treatment of COVID-19 and only handful more are under an Emergency Use Authorization (EUA), which is used for drugs that have not been FDA approved or are being used for an unapproved circumstance(4). Therefore, it is important to find new drugs that could help lessen symptoms and mortality rates for COVID-19 while ensuring they are safe to use. This project provides a retrospective

analysis of the safety and efficacy of three Amgen COMMUNITY drugs used during the Amgen study at the Sunbeam site from December 2020 through April 2021 in patients aged 55 to 86 who were hospitalized with COVID-19 and required oxygen or ventilation.

Materials and Methods

Retrospective data was pulled on each patient to determine the safety and efficacy of the study. This data was stored on Real-Time and originally gathered from hospital records, in-person patient visits and telephone visits. A total of 28 patients enrolled in the study and either completed the treatment phase or passed away during it. These patients were randomized into three different arms: Apremilast, Lanadelumab, and Zilucoplan.

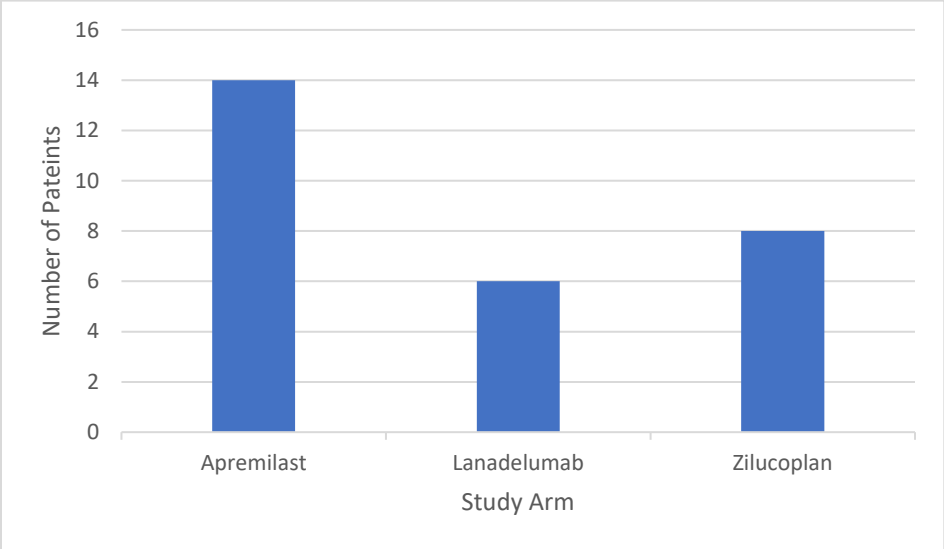

Figure 1. Number of patients randomized to each study arm.

Each patient's fit-to-discharge value on the day of discharge/death and day 29 was pulled to determine efficacy. Day 29 was considered to be the end of the treatment period

unless a patient was discharged earlier or was deceased. The fit-to-discharge scale ranges from 1 to 8 (Appendix A), where a 1 indicates death and an 8 is discharged without complication. Therefore, successful treatments would have an ordinal rank of 7 or 8 on the day of discharge or end of treatment. A Kruskal-Wallis test was used to determine the efficacy of the three drugs in comparison to each other since the data was non-parametric, ranked data.

Data was collected on the number of adverse and serious adverse events that occurred, as well as the grade of each event, to assess the safety of the study. Adverse and serious events were also ranked on a grading scale from 1 to 5(Appendix B) to assess the severity of the event. Once again, a Kruskal-Wallis test was used to compare the total number of adverse and serious adverse events for each drug as well as the number of each grade of event that occurred. A Kruskal-Wallis test was used because this data is also non-parametric, ranked data.

Results

To assess the efficacy of the study, the percentage of patients that were ranked a grade 1 overall and in each study arm was assessed. Then each of the three drugs were compared via a Kruskal-Wallis test to determine if they were equally as efficacious to each other or if one was more efficacious than the rest. 13 patients were taking Apremilast, 6 were taking Lanadelumab, and 8 were taking Zilucoplan. Of the 28 patients, 50% had an ordinal rank of 1 at the end of treatment. Apremilast and Lanadelumab had 50% of their patients with an ordinal rank of 1 at the end of the study treatment, while Zilucoplan saw only 37% of patients with an ordinal rank of 1 during the study. The ordinal number assigned to the patient on the

day of discharge/death or day 29 was used to compare the efficacy of each drug in relation to one another.

Patient Study Drug Assignment with End of Treatment Ordinal Rank

Patient	Study Arm	Ordinal Rank	Patient	Study Arm	Ordinal Rank	Patient	Study Arm	Ordinal Rank
1	Apremilast	4	14	Lanadelumab	1	25	Apremilast	1
2	Apremilast	7	15	Lanadelumab	8	26	Apremilast	1
3	Apremilast	1	16	Zilucoplan	1	28	Zilucoplan	1
4	Apremilast	1	18	Lanadelumab	1	30	Zilucoplan	8
5	Apremilast	2	19	Lanadelumab	8	32	Zilucoplan	8
6	Apremilast	8	20	Apremilast	1	33	Lanadelumab	8
7	Apremilast	8	21	Zilucoplan	8	34	Zilucoplan	8
8	Apremilast	8	22	Apremilast	1	36	Zilucoplan	8
9	Apremilast	1	23	Zilucoplan	1			
13	Apremilast	7	24	Lanadelumab	1			

Table 1. Table showing which arm each patient was randomized to and their ordinal rank at the end of treatment, which was either day 29 or the day of discharge.

The null hypothesis for the Kruskal-Wallis test is that all three drugs are equally as effective. The test was run using SPSS Statistics software and found a test statistic(H) of 1.589, leading to a significant value of 0.452 with an alpha value of 0.05.

Test Statistics[a,b]

	Ordinal
Kruskal-Wallis H	1.589
df	2
Asymp. Sig.	.452

a. Kruskal Wallis Test

b. Grouping Variable: Drug

Table 2. SPSS Statistics output to compare the efficacy on Apremilast, Lanadelumab and Zilucoplan

Data was pulled on the adverse and serious adverse events to assess the safety of the three drugs. The figure below shows the amount of adverse and serious adverse events for each study arm.

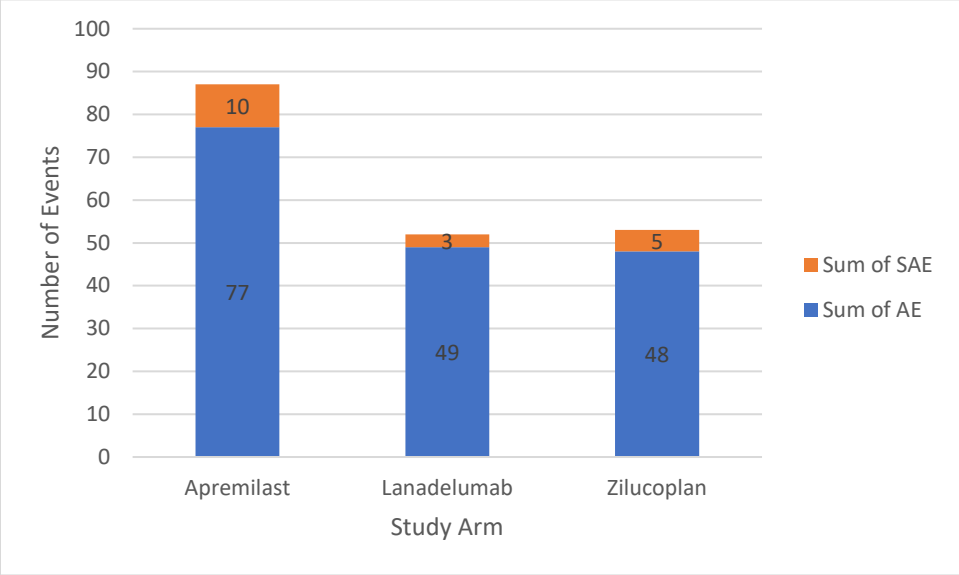

Figure 2. Count of adverse and serious adverse events per study arm

In addition, the number of each grade of adverse event per drug was also pulled. The figure below shows the amount of each grade of event per study arm.

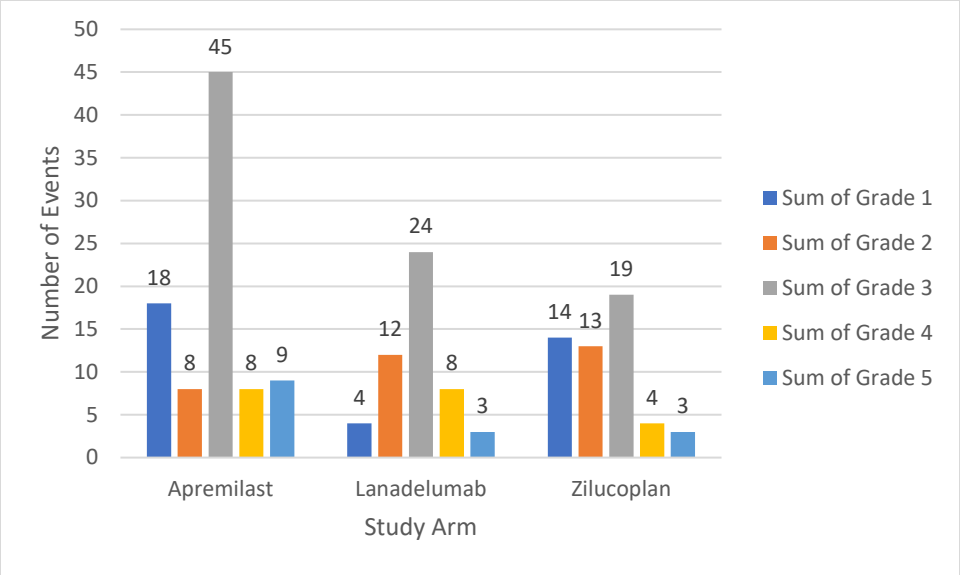

Figure 3. Count of each grade of adverse and serious adverse events per study arm

Multiple Kruskal-Wallis tests were also run to determine the safety of the drugs. The null hypothesis is that all the drugs are equally as safe. The tests were run using SPSS Statistics with an alpha value of 0.05 for all tests. For adverse events, the test statistic was 0.716, with a significance value of 0.699. For serious adverse events, the test statistic was 0.976, with a significance value of 0.614. The test statistic for Grade 1 was 1.326, with a significant value of 0.515. Grade 2 had a test statistic of 0.147 giving a significant value of 0.147. Grade 3 had a test statistic of 0.356 leading to a significant value of 0.837. Grade 4 had a test statistic of 0.383 which gives a significant statistic of 0.826, and lastly, grade 5 yielded a test statistic of 1.454 which gives a significant value of 0.483.

Test Statistics[a,b]

	AE	SAE	Grade1	Grade2	Grade3	Grade4	Grade5
Kruskal-Wallis H	.716	.976	1.326	3.836	.356	.383	1.454
df	2	2	2	2	2	2	2
Asymp. Sig.	.699	.614	.515	.147	.837	.826	.483

a. Kruskal Wallis Test

b. Grouping Variable: Drug

Table 3. SPSS Statistics output to compare the safety of each drug based on adverse and serious adverse events and their grade.

Discussion

To determine the efficacies of the three drugs, the percentage of patients who died and the efficacy of the drugs in comparison to each other were assessed. A Kruskal-Wallis test was done to determine the efficacy of the three drugs. Patients' ages ranged from 55 to 86, and all patients required non-invasive or invasive ventilation when they started taking one of the study medications. Of the 28 patients 18 were Caucasian males, 8 were Caucasian females, 1 was a Black female and 1 was an Asian female. The most prevalent comorbidities were Diabetes, Chronic Pulmonary Obstructive Disorder(COPD) and cardiovascular diseases, such as hypertension and hyperlipidemia. Of the total patients in the study, 13 suffered from COPD, 11 suffered from diabetes and 26 suffered from hypertension and/or hyperlipidemia. Overall, 50% of patients died while taking the study medication, and the cause of death was found to be due to COVID-19 in all cases. This percentage of death is similar to that of patients who die from COVID-19 associated ARDS, which is 45%(12). Since the significant value from the Kruskal-

Wallis test was 0.452, we failed to reject the null hypothesis that all drugs are equally as efficacious. Even though Ziluocplan seemed to have less patients with an ordinal rank of 1, this was not statistically significant due to the results of the Kruskal-Wallis test; therefore, we must accept the null hypothesis that all three drugs are equally effective meaning that none of the drugs were found to be very efficacious.

The safety of the three drugs was assessed by looking at the number of adverse and serious adverse events that occurred for each drug. Each adverse and serious adverse event were also ranked on a grading scale from 1 to 5. This was assessed using a Kruskal-Wallis test. The null hypothesis is that all three drugs are equal in safety. For overall adverse and serious adverse events, the test statistic was more than the alpha value of 0.05; therefore, we failed to reject the null. This concludes that there was no statistical significance in the amount of adverse and serious adverse events per drug. The same was true for each grade of an adverse or serious adverse event. No statistical significance was found so each drug was equal in the grade of an events that also occurred. In the data pulled, adverse events were assessed by the investigator to determine if there was a possibility that it occurred due to the study drug or if it was due to an underlying disease. Only one adverse event, ranked a grade 1, was determined by the investigator to have a reasonable possibility of being related to the drug due to previous knowledge of known drug side effects. All other adverse events were in relation to COVID-19 disease progression or other underlying health issues. Since the investigator rarely determined adverse events to be related to the study drugs and the drugs were all equal in their safety, it can be assessed that all three drugs were safe to use and did not cause any significant unwanted side effects compared to the disease progression of COVID-19.

Conclusion

In conclusion, there is a need for continuing research on drugs to treat COVID-19 and the respiratory symptoms associated with it. All three of these drugs were found to be safe with limited side effects. The potential benefit of taking the drug far outweighed any associated risk, and almost all adverse and serious adverse events were due to COVID-19 disease progression or an underlying disease.. Even though it can be concluded that the study was safe, the drugs were found to be relatively ineffective. There was no statistical difference in the efficacy of the three drugs, and the overall percentage of patients who died was similar to that of patients who died after developing ARDS. Since these drugs were not found to be very efficacious, it is necessary for continued research to find more drugs that are not only safe but effective in combating COVID-19, especially when patients are far into the disease progression. COVID-19 is a new reality for the world, and it is essential for the development of more treatments moving forward.

CHAPTER III: Internship Experience

I completed my internship at Sunbeam Clinical Research. Sunbeam is a small site management organization (SMO). Sunbeam is the liaison between the primary investigator for trials and the contract research organization(CRO) or Sponsor. As an SMO, they have multiple sites with various primary investigators. They send a research coordinator to each site to manage the studies that are active there. I spent most of my time at sunbeam learning about clinical research coordinator tasks and business development.

Most of my days consisted of assisting the research coordinators with study visits and regulatory work. I spent time at three different sites and worked on about five different studies. I started at the Greenville site working on the Galderma and Cara studies. I assisted with patient visits which included collecting patients medical history, taking vitals, taking ECG and helping to dispense and administer IP. Patient also had labs drawn at each visit so I helped with preparing the samples and shipping them out as defined in the study laboratory manual. I also educated patients on the use of their handheld devices that presented them with daily questionnaires. Shortly after, both the Galderma and Cara study were started at the site in McKinney so I assisted at that site as well. In December, I got moved over to the Sunnyvale site to work on V-Inception. I consented patients and educated them on the study. I also collected their medical history and did data entry in RealTime and on the sponsors Electronic Data Capture (EDC) system for each patients visits. This study also required labs at each visit so I assisted in preparing and shipping the samples according to the lab manual. At the Sunnyvale site, I also ensured that all regulatory documents were kept up-to-date which included temperature

monitoring, ensuring all logs were updated and that IRB approval was up-to-date. I also spent a lot more time in communication with the study doctor in order to identify potential patients and recruit them to join the study.

While assisting with research coordinator responsibilities, I also worked on business development. I searched for new studies and would reach out to sponsors to see if they would add one of Sunbeams investigators on as another site. I also learned how to fill out regulatory documents that are needed for a study start-up and attended some site initiation visits.

During my internship, I also worked on this internship project. The data from the COMMUNITY study was stored in RealTime where I was able to pull all the necessary data for this project. In-between assigned site duties, I was able to work on background research, statistical analysis and the collection of data from RealTime.

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Appendix A

Clinical Severity Status 8-Point Ordinal Scale (1)

1.Death

2.Hospitalized, on invasive mechanical ventilation or ECMO

3. Hospitalized, on non-invasive ventilation or high-flow oxygen devices

4. Hospitalized, requiring supplemental oxygen

5. Hospitalized, not requiring supplemental oxygen, requiring ongoing medical care

6. Hospitalized. Not requiring supplemental oxygen, no longer requires ongoing medical care

7. Not hospitalized, limitation on activities and/or requiring home oxygen

8.Not hospitalized, no limitations on activities

Appendix B

CTCAE Grading Scale (13)

Grade 1: Mild-asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated

Grade 2: Moderate- minimal, local or non-invasive intervention indicated; limiting age-appropriate activities

Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care

Grade 4: Life threatening consequences; urgent intervention indicated

Grade 5: Death

Appendix C

Internship Journal

8/22/22: Completed Good Clinical Practice training and uploaded to my profile in CTMS.

8/23/22: Completed dangerous goods shipping and HIPPA trainings. Uploaded documents to my profile on CTMS. Completed training on the use of RealTime, our CTMS system. Then I updated my CV with my completed trainings and uploaded it to my CTMS profile. Also, we discussed the different areas in clinical research and where Sunbeam fits in:

Sponsor→CRO→SMO(us)→PI/Site→Patients

8/24/22:

Completed trainings in Canvas that covered GCP, ICH, FDA guidelines, clinical research ethics and basics of clinical research.

8/25/22: Went to Fort Worth today to work on the MD True Care study (Alto-100) which deals with patients with mental disorders(MDD, PTSD). Saw a patient for their Visit 1 today and learned how a baseline visit is conducted. I practiced entering data into RealTime and assisted with taking the EEG.

8/26/22: Today I called the patient to finish questions from the baseline visit and to let her know that her payment card was active. Then I reviewed the ICF and Protocol for the Galderma study.

8/29/22: Today I completed a screening visit for the Cara study. We went over inclusion/exclusion. I learned how to identify potential patients for the study, how to record and report an SAE, and how to close a query from lab results.

8/30/22: I assisted with a patient visit over the phone for the Alto study. We asked the patients some questions about how they were feeling since taking the medication. I set up supplies for a baseline visit for Cara. Then we went to Dr.Butt's office to go over the Galderma study. He gave us three potential patients for pre-screening.

8/31/22: Today I trained on how to use RealTime. I reviewed the protocol and ICF for the Galderma study. I assisted with an EKG during a screening visit for Cara. I also helped with preparing labs for shipment and learned how to obtain informed consent from a patient. Then I entered in patients profiles and scheduled them for pre-screen.

9/01/22: Today I conducted a Day 1 visit for Cara. I learned how randomization worked for this study. I assisted with EKG, preparing and shipping labs, taking vitals and dispensing medication. Then I learned how they update RealTime and EDC for the visit.

9/02/22: Today I did my training for Galderma so that I could be added to the delegation log. Then I spent the day looking for possible new studies on clinicaltrails.gov. I also worked on my research proposal.

9/06/22: Today I set up lab kits for patient visits for tomorrow. Then I reviewed the AMGEN COVID protocol to work on my proposal.

9/07/22: Today I assisted with randomization for 840015-002. I took vitals, helped with EKG and prepped labs for shipment. Then I assisted with data entry. Then, I learned how a run-in visit worked. I assisted with registering the device and then training the patient on its use.

9/08/22: Today I learned how to unpack and log IP shipments. Then I trained another Cara patient on how to use their device to complete questionnaires.

9/09/22: We received a shipment of new lab kits and requisition binders. I learned how to log those on RealTime. I consented a patient for the Cara study and reached out to a sponsor for a possible new study.

9/12/22: I prepared the lab kits for patient screening and baseline visits for Cara and then uploaded regulatory documents into RealTime. I called multiple patients to schedule and confirm visits. Then I updated temperature logs.

9/13/22: Today I just looked for new studies and reached out to sponsors for multiple Sunbeam PI's. Then I reviewed the protocol specifics for each drug in the AMGEN study and went over the RealTime data.

9/14/22: Today there was a screening visit for Galderma. I assisted with preparing and shipping the patients labs and performing the EKG. I learned how to do PEF and then I entered the data into RealTime.

9/15/22: Today we had a monitoring visit(IMV) for Cara. I learned what happens during one.

9/16/22: We re-did the EKG and PEF for the patient from the other day. I assisted with those again. Then we randomized patient 840015-004. I took her vitals, assisted with the EKG and prepared and shipped her lab samples. I then entered data into RealTime

9/19/22: Today I did training on the ERT ePRO devices for Cara. I also trained on how to use the EKG machine and transmit the data to ERT.

9/20/22: I worked on my research proposal by doing some background research on COVID and the three drugs used in the trial.

9/21/22: Today we were notified of an SAE. I helped fill out the appropriate forms and sent it off to the sponsor. This was documented in RealTime and in EDC.

9/22/22: We had two SAE's that we were made aware of today. I spent the day filling out the appropriate documents and talking with the monitor and sponsor.

9/23/22: Today I assisted with consenting a patient into the Galderma study. I set the patient up with her ePRO device to be able to do her daily questionnaires and trained her on how to use it. I reviewed the patient documents for Galderma to prepare for the coming monitor visit.

9/26/22: Patient 9977-006 had his follow-up visit today. The patient refused to give labs or have his ECG done. Patient ePROs were completed and patient agreed to come in on Friday to complete his visit.

9/27/22: Today we screened a patient for Cara. The patient's medical history was collected and reviewed. I took patient vitals and assisted with ECG and lab preparation and shipment. All data was entered into RealTime and EDC.

9/28/22: Today I met with a new contracted PI. We trained him on RealTime and obtained information about his practice and patient population. I learned about business development and what goes in to setting up a new site. I also completed my training for Medidata which is the EDC for Galderma.

9/30/22: Today we had a monitor visit for Galderma at Dr.Ijaz.

10/03/22: Today I helped to identify potential patients and pre-screen patients for the upcoming week.

10/04/22: This morning I woke up with a sore throat so I worked remotely. I looked for new studies and sent out emails. I also updated regulatory documents for both studies at Dr.Ijaz's. Then I spent some time with customer support for the ePRO devices for Cara to work out a glitch with the End of Week 4 visit questionnaires.

10/05/22: Patient 977-007 had his follow up visit today. Labs were collected and I helped to prepare and ship the samples. Then, patient 840015-004 had her End of Week 4 visit. Her vitals were taken and I helped her complete her ePROs on her device. Then I prepared and shipped her lab samples. All data was entered into RealTime and the relevant EDC for each visit.

10/06/22: Today I consented a patient to the Cara study and helped complete their screening visit. Patient medical history was collected, vitals and ECG were done. Then I helped to prepare and ship lab samples. All the data was entered into RealTime and the EDC.

10/07/22: Today there was a staff meeting to discuss business development. We went over how to search for new studies and how to reach out to sponsors. Then I completed inventory in the head office.

10/10/22: Today patient 9977-012 was randomized. I helped to prepare and ship her labs. The I helped her complete her ePROs and we took her PEF. All the data was entered into RealTime and EDC. Patient was unable to be administer IP due to her ACT score being too low.

10/11/22: Today I spent the day looking for new studies for Dr.Ijaz's site. I finished up data entry int EDC from the previous days visit and helped communicate with the monitor to see if we could re-screen the patient once her asthma was controlled and her ACT score reflected that.

10/12/22: Today, patient 840015-007 had her run-in visit. I trained her on the use of her device and completing ePROs at home. I entered the data for this visit into RealTime and the EDC.

10/13/22: Today was spent assisting in answering queries for Galderma and Cara on the EDC.

10/14/22: Today we finished responding to all queries. Then I spent some time looking for new studies and working on my internship project.

10/17/22: Today we completed a screening visit for Cara. Patient medical history was collected. Vitals, ECG and labs were taken. I assisted with the preparation and shipment of lab samples. All data was entered into RealTime and the EDC. I contacted patients to scheduled their upcoming visits as well.

10/18/22: Today I helped fill out an SAE report for patient 9977-006. I identified potential patients for the rest of the week and set up the incubator at Dr.Butt's office. I completed my ePIP training which is the site for Galderma where the medical monitor approves patients randomization and can answer any other medical questions that may arise in relation to the study.

10/19/22: Today we screened a patient for Cara. Patient medical history was collected. Vitals, ECG and labs were taken. I assisted with the preparation and shipment of lab samples. All data was entered into RealTime and the EDC. The patient 840015-007 was randomized. I took her vitals and helped her complete her ePRO's. Then I assisted with her ECG and preparing and shipping lab samples. She was then randomized and dispensed IP. Data was entered into RealTime and EDC for both visits.

10/20/22: Today I helped file regulatory documents and had a run-in visit for a Cara patient. I trained them on the use of their device and how to complete their ePROs daily at home.

10/21/22: Today I helped resolve queries and contacted patients to schedule their visits. Then we identified more potential patients.

10/24/22: Today patient 9977-012 was able to be randomized. I helped her complete her ePROs and I assisted with preparing and shipping her lab samples. After her dialysis, PEF was taken and her IP was administered. All visit data was entered into RealTime and EDC.

10/25/22: Today we learned of another SAE for patient 9977-006. I helped with filling out the report forms and filling the documents.

1-/26/22: Today we screened a patient for Galderma at Dr.Butt's. I took vitals and assisted with ECG. I also trained patient on the use of device and completing ePROs. Then I helped prepare and ship the lab samples. All data was entered into RealTime and the EDC.

10/31: Today we screened a patient for Cara. Medical history, vitals, ECG and labs were taken. I assisted with preparing the samples and shipping them. All data was then entered into RealTime and the EDC.

11/01/22: Today we prepared for our upcoming monitoring visit. We went through all regulatory documents to make sure they were up to date and went through patient data to ensure that there were no entry errors.

11/02/22: Today we had patient 840015-002 End of Week 8 visits. Vitals were done and I helped him with his questionnaires. Then I assisted with the preparation and shipment of lab samples. Patient 840015-010 had her run-in as well and I trained her on use of the device and how to complete here daily ePROs. Data was entered into RealTime and EDC for both visits.

11/03/22: Patient visits were updated in order to prepare for the upcoming monitor visits. Then, we spent the day looking for more potential patients that would fit the new protocol amendment for Cara.

11/04/22: Today a patient was screened at Dr.Butt's. I took his vitals and assisted with his ECG. Then I prepared and shipped his labs samples. I helped train him on the use of the device and

how to complete daily ePROs. All data was entered into RealTime and the EDC. Then, we had a virtual monitoring meeting for Cara.

11/07/22: Today I started screening a patient for Galderma. I took their medical history down and went over it with the patient.

11/08/22: Today I completed my trainings for Veeva Vault which is the EDC for Cara.

11/09/22: Today was a baseline visit for 840015-010. Vitals, ECG and labs were done. I helped prepare the lab samples and assisted the patient in completing her ePROs for the visit. She was randomized and dispensed IP. Then all data was entered into RealTime and the EDC.

11/10/22: Today was a baseline visit for 840015-009. Vitals, ECG and labs were done. I helped prepare the lab samples and assisted the patient in completing her ePROs for the visit. She was randomized and dispensed IP. Then all data was entered into RealTime and the EDC.

11/11/22: I spent the day sorting boxes of old records from previous studies. I organized piles to keep and then went through the destroy piles to separate into either shred or trash.

11/14/22:Today I spent the day sorting through records again.

11/15/22: I again spent the day sorting through records.

11/16/22: Today we had a monitoring visit for Galderma at Dr.Ijaz's

11/17/22:Patient 9977-010 had her Week 12 visit previously. I assisted with completing data entry into the EDC from RealTime and our source documents

11/18/22: Today I finished sorting boxes and then spent some time looking for new studies.

11/21/22: Patient 9977-012 had her week 4 visit today. I helped to prepare and pack the lab specimens. I also assisted the patient with completing her ePRO's and assisted with IP administration. I took the patients PEF as well and then helped enter all data into RealTime and the EDC.

11/22/22: Today patient 840015-003 had her end of treatment visit. We took vitals and did her ECG. Then I helped with preparing and shipping labs. We discussed moving the patient into the long term extension phase but she did not want to continue. We collected her old IP and entered all the data into RealTime and EDC.

11/23/22: Today I was at the head office. I helped finish entering data from the previous day's visits into EDC. Then I spent the day looking for new studies and emailing sponsors to see if any of Sunbeam's investigators were able to become a site for their studies.

11/24/22: Thanksgiving Holiday

11/25/22: Holiday

11/28/22: Had an SQV for Cara today.

11/29/22: Had an unscheduled visit and run-in visit for Cara today. Updated EDC and RealTime for two Cara patients who experienced AE's. Responded to queries for Cara to prep for monitor visit. Came to new head office to unpack and set up for Dr. Butt monitor visit. Registered for IRB access for Dr. Khan.

11/30/22: Prepped for Cara and Galderma monitoring visits. Reviewed all data in CTMS and EDC was correct. Then packed old office in preparation to move.

12/01/22: Had an IMV for Cara today and worked on my project.

12/02/22: Randomized patient 9977-013 for Galderma today. Processed labs, took PROs, performed PEF testing on patient and then administered IP via injection.

12/05/22: Randomized patient 7022-003 for Galderma today. We collected and processed labs, did ediaries with patient, took PEF and administered the medication via injection. All data was recorded in CTMS and then transferred to the EDC. I emailed sponsor contacts for new studies and helped unpack the new office.

12/06/22: Patient 840015-011 was randomized today. We took and processed labs, performed ECG and took vitals. IP was administered. All data was recorded in CTMS and then EDC. I then assisted with setting up CTMS regulatory documents for a new study.

12/07/22:Today patient 840015-004 had her end of treatment visit. We took her vitals and ECG. I assisted with preparing and shipping the lab samples. We also completed all ePRO's with the patient. Since she wanted to be enrolled in the extension phase, we re-randomized her and dispensed new IP. Then, patient 840015-010 had her end of week 4 visit. Her vitals and labs were collected. I assisted her with her ePROs and with preparing and shipping the lab samples. IP accountability and dispensation were completed.

12/08/22: Today, patient 840015-009 had her end of week 4 visit. Vitals were taken and I assisted with ePROs. I also prepared and shipped her lab samples. IP accountability and dispensation were completed. Data was entered into RealTime.

12/09/22: Today was spent catching up on data entry. We finished updating RealTime and then entered all data into the EDC from the previous couple days of visits. We also scanned and uploaded documents that had been signed by the Dr. Ijaz.

12/12/22: Went to Dr.Ali's office to see a potential patient for V-inception. Completed the training and delegation logs for all studies at this site. Patient was consented and scheduled to come in the next day for her blood draw as she was not fasting. Her patient profile was created in RealTime, and her ACS Index event information was obtained and documented in RealTime.

12/13/22: Went to Dr.Ali's again today to complete previous days patient visit. She ended up not coming in due to the storm. We rescheduled her for Thursday. The rest of the day was spent gaining accesses to necessary study sites.

12/14/22: Today we were at Dr. Ijaz's office. We went over regulatory documents for all studies occurring there. We also uploaded signed documents from the previous weeks visits and identified potential patients for next week.

12/15/22-12/20/22: Had COVID

12/21/22-12/30/22: On Holiday. Worked on Internship project during this time.

01/03/23: Patient 1135-004 was rescheduled for her blood draw. Then temperature monitoring was done for the previous week. There was a non-permissible excursion so paperwork was filled out and excursion was reported to the sponsor. I replied to emails that were sent over the

holiday and then worked on statistical analysis for my project. I also got resolved queries for V-Inception and requested accesses for IWRS and ePROs for Cara at Dr. Butt's.

01/04/23: Patient 1135-004 came in for her blood draw. I processed her labs and prepped them to be shipped out. I then registered the visit in IRT and updated RealTime. I also updated her medical and surgical history and then registered her in EDC.

01/05/23: Patient 840015-002 came in for his End of Week 4 Period 2 visit. We took his vitals and then they took labs. I processed the labs to be ready to ship out and them completed the visit in RealTime. Then we drove back to the head office to discuss patient 1135-004. She had been hospitalized over Christmas and we were unsure if she still qualified for the study. They decided to have her sign a new consent from the date of blood draw and to still use her previous MI as her index event.

01/06/23: Started at the head office and got the labs for patient 1135-004. She was a screen-failure. I helped to set up decorations in the new office. Then I drove to Dr. Ijaz's where there was a potential patient for Cara. I consented the patient, took vitals, assisted with ECG and prepared the labs for shipment. I then updated RealTime, EDC and IWRS with the visit information. I also followed up with the temperature excursion at Dr. Ali's site.

01/09/23: Today I came to Dr. Ali's site to meet with patient 1135-004. She never showed up, so I left her a voicemail. I am awaiting instructions on how to move forward with data entry. I did temperature monitoring and attended a virtual meeting for OPT-BB.

01/10/23: Today I uploaded some documents for V-Inception. Then I worked on resolving queries for Galderma and prepped for the IMV on Thursday. I ensured that source and EDC data were correct and that queries were resolved. Patient 840066-001 was screened. We took informed consent, obtained medical history, did EKG and prepared and shipped labs.

01/11/23: This morning I finished audit prep for the IMV visit tomorrow. Then I finished uploading documents for yesterday's patient visit. Patient 9977-010 had her follow-up. We prepared and shipped her lab samples and then had her fill out her ePROs. Patient 9977-012 had an unscheduled visit to recollect her hematology, so we sent packed and shipped that after collection.

01/12/23: Today we had an IMV for Galderma at Dr.Ijaz's in Greenville.

01/13/23: I went to Sunnyvale because we received an IP shipment. I unpacked it and checked to ensure that it was within the proper temperature and no kits were damaged. I logged the shipment in RealTime. Then I completed the Data Change Form for patient 1135-004 so that I can finish entering her screening data into the EDC. Then I spent time working on my internship project.

01/16/23: I entered medical history data for patient 9977-014 into EDC this morning. Then the rest of the day was spent doing audit prep for the Cara IMV. I also looked for new studies and reached out to sponsors. I received one reply and was able to give them patient population demographics. They are going to discuss adding Sunbeam as an additional site.

01/17/23: Today I completed audit prep for Cara IMV tomorrow. I uploaded old documents int RealTime. Then I met the new intern and went overlooking for new studies with her.

01/18/23: Today we had a monitoring visit for Cara. Patient 9977-012 had her End of Week 12 visit. I helped prepare labs, do EKG and PEF. All data was entered into Realtime and EDC for the patient visit.

01/19/23: Today the monitoring visit for Cara was completed. We responded to queries on RealTime and in the EDC. We uploaded all regulatory documents from the visit as well.

01/20/23: Today I was at Dr.Ali's office to prepare for a patient visit on Monday and two potential patients. I obtained their hospital records so I could start data entry of their medical history and Index MI information.

01/23/23: Today I was at Dr.Ali's office again for patient visits. We screened one patient and I assisted with preparing the labs to ship out. I also entered all the visit data into RealTime and the EDC. Then, I sat in on a meeting with the PI regarding the study and the role of coordinators. After that, patient 1135-001 had their Visit 3. Labs were collected and I helped prepare all of those to ship. All the visit data was then entered into RealTime and the EDC.

01/24/23: Today I caught up on some data entry for V-Inception and responded to queries in the EDC. Then, a potential patient came in for Cara at Dr. Butt's office.

01/25/23: Today patient 840015-012 had his Baseline visit. Vitals, ECG and labs were collected. I took vitals and assisted with lab sample preparation and shipping. I entered all data into RealTime and EDC. Then, we had a remote monitor visit for V-Inception. Regulatory documents

were updated accordingly. Then I had a meeting with Dr.Nandy to review my statistics for my project.

01/26/23: Today I came to Dr.Ali's to finish data entry for a patient. I then worked on my project the rest of the day.

01/30/23: Today I came to the head office for patient 7022-004 end of week 8 visit. I assisted with preparing and shipping lab samples. Then I entered all data into RealTime and EDC. Today I left early due to the coming storm.

01/31/23: Closed due to ice storm.

02/01/23: Closed due to ice storm

02/02/23: Today I worked from home due to the ice storm and driving conditions. I responded to emails and updated data in RealTime and the EDC for V-Inception. I also looked for future studies and sent out some emails for those.

02/03/23: Today I went to Dr. Ali's office to consent a potential patient. The patient agreed so we filled out all required paperwork and then scheduled the patient for a follow-up visit to complete study procedures such as labs and ECG since samples could not be shipped due to the ice storm.

02/06/23: Today I consented patient 1135-008. All paperwork was filled out. ECG and vitals were done and I assisted with preparing and shipping the lab samples. Then I entered all data

into RealTime and the EDC. Patient 1135-006 returned to finish his screening visit. I assisted with preparing and shipping those labs and entered all the data into RealTime and EDC. I finally got hospital records for four V-inception patients so I spent the rest of the day entering that information into RealTime.

02/07/23: Today I came to the head office and worked on completing data entry from yesterday. I also scanned and uploaded source documents.

02/07/23: Today's patient did not show so I rescheduled him for next week. I uploaded some patient documents and prepared for tomorrow's patient visit. I also did some general house-keeping and cleaning around Dr.Ali's office.

02/08/23: Today I came to Sunnyvale at Dr.Ali's office. The patient rescheduled again for next week. I got lab results back for patient 1135008 and he had exclusionary results, so I updated him to screen failure on RealTime, Cenduit and the EDC.

02/10/23: Today we had a staff meeting at the head office. We did a training on business development and then went over challenges and successes at each site.

02/13/23: Today I went to Dr.Ali's in Sunnyvale. I did temperature monitoring and updated the regulatory logs. Then, I spent time emailing the sponsor lab due to them missing samples. The rescheduled potential patient came in for his visit with Dr.Ali and I sat down with him and went over the study and the Informed Consent paper. The patient was unsure about participating so I

sent him home with the consent form and a pamphlet to have adequate time to consider joining the study.

02/14/23: Today I went to the head office and helped the other coordinators catch up on data entry from the last few days. I also responded to emails to work out a mix up with a patients lab samples. Then, I worked on my internship project and spent the last hour searching for new studies and reaching out to sponsors.

02/15/23: Today I worked on writing the materials and methods section of my internship project. Then I looked for new studies for Sunbeam and sent out emails.

02/16/23:Today I did audit preparation for the upcoming Cara monitoring visit. I also spent the day in correspondence with the V-Inception monitor to try to figure out what happened with the central laboratory and why our patients lab samples are missing. Then, I looked for potential studies and reached out to sponsors.

02/17/23: Today patient 840066-002 came in for their baseline visit. We took vitals and ECG and then went over questionnaires with him. We registered the visit to dispense medication and trained him on medication compliance. Then I assisted with preparing and shipping the lab samples. Patient 7022-002 had to come back to re-draw labs. I also helped with preparing and shipping his samples. Then all data was entered into RealTime and the EDC.

02/20/23: Today I went to Dr.Ali's. I did temperature monitoring and then finished some data entry of hospital records for patients. I also consented a patient for OPT-BB and collected her medical history.

02/21/23:I was out sick with the flu today but offered guidance on completing the scheduled patient visit and what data entry needed to be done.

02/22/23: I was out sick with the flu today and worked on my project.

02/23/23: I was out sick with the flu but worked on editing my paper for my project.

02/24/23:I was still sick with the flu but I answered emails from home and offered guidance on data entry from the patients visits.

02/27/23: Today I went to Dr.Ali's. I scheduled patients visits for the week and worked on data entry into RealTime and EDC for patient visits that occurred last week while I was out sick. I also caught up on responding to emails that I missed while I was out sick.

02/28/23: Today I came to the head office. There was a patient visit for 840066-003. We did his EKG, vitals and questionnaires. I assisted with preparing and shipping his lab samples as well. Then he was randomized and we dispensed IP. Then patient 840066-002 came in to have his blood redrawn. I assisted with preparing and shipping the samples. I then had a virtual meeting for V-Inception that went over study progress.

03/01/23: Today I went to Dr. Ali's office. Patient 1135003 had her Visit 3 for V-Inception. I took her vitals and updated her medical history. I assisted with preparing and shipping her lab samples as well. All visit data was entered into RealTime and the EDC. She was also administered medication. Then patient 1135006 came in for his baseline visit. I took vitals and I assisted him with completing his questionnaires. Then I helped with prepping and shipping his

lab samples. He was randomized to usual care, so his visit ended after that. Then I entered the data into RealTime and EDC. After that, I finished collecting data for the OPT-BB patient from Dr.Ali's EMR. Also, a new CRC started so I went over the protocols for all the studies being conducted at Dr.Ali's with him.

03/02/23:Today I went to Dr.Ijaz's office. Patient 840015-009 had her End of Week 4 extension visit. I helped her with questionnaires and took her vitals. Then I helped prep and ship her lab samples and we dispensed her new medication. Then, patient 840015-002 had his End of Week 12 extension visit. I took his vitals, did his questionnaires with him and helped prep and ship his lab sample. He was dispensed new medication as well. Then all data was entered into RealTime and the EDC. After this, I helped with resolving some queries in the EDC about SAE's that had previously occurred for two Cara patients.

03/03/23: Today we had a team meeting at the head office. We went over how to complete a regulatory packer for the start of a study. We also went over how to do an ECG. Then I worked on completing my project and responding to emails from sponsors.

03/06/23-03/17/23: I prepared and practiced my presentation for my defense.

03/20/23: Project Defense at 11AM