# 

# DSMB Report

Project Title: Lovastatin Clinical Trial

PI: Randi Hagerman, MD

2nd DSMB Meeting: 8/14/2017

Date of report: 8/ 3/2017

Data as of: 7/28/2017

Prepared by: Kyoungmi Kim, PhD

Division of Biostatistics

UD Davis School of Medicine

**Section 1. Recruitment and Participant Status**

**Figure 1. Enrollment and Accrual of Study Participants (as of 7/28/2017)**

Twenty three participants were recruited for the Lovastatin Clinical Trial. Twenty two enrolled in the trial and one failed screening. Twenty two participants were blindly assigned to either Group A or B. As of 7/28/2017, the AE data are available for 22 enrollees.

**Figure 2. Overall Study Status**

Table 1. Participant Enrollment Status

|  | **N** | **%** |
| --- | --- | --- |
| **Screened** | 23 | 100 |
| Screen Failed | 1 | 4.4 |
| **Enrolled (randomized)** | 22 | 95.6 |
| Active | 5 | 21.7 |
| Completed | 15 | 65.2 |
| Early Termination | 2 | 8.7 |
|  |  |  |
| **Discontinued from Study** |  | 0 |
| Lost to follow- up | 0 |  |
| SAE/AE | 0 |  |
| Withdrew Consent | 0 |  |

### Table 2. Reasons for Screen Failures

| **Reason** | **Total N** | **Total %\*** |
| --- | --- | --- |
| Disqualified due to high IQ | 1 | 4.4 |
|  |  |  |
| **Total Screened** | 23 |  |
| **Total Screen Failures** | 1 | 4.4 |

### \* - % of the total number screened

### Table 3. Demographic Characteristics of Enrollees

| **Characteristics** | | **All N (%)** | **Group A N (%)** | **Group B N (%)** | **Group Difference P-value\*** |
| --- | --- | --- | --- | --- | --- |
|  |  |  |
| **Total Enrolled:** | | 22 |  |  |  |
| **Gender** | Male | 21 (95.5%) | 10 (90.9%) | 11 (100%) | 1 |
| Female | 1 (4.5%) | 1 (9.1%) |  |
| **Ethnicity** | Hispanic or Latino | 3 (13.6%) |  | 3 (27.3%) | 0.0902 |
| Not Hispanic or Latino | 18 (81.9%) | 11 (100%) | 7 (63.6%) |
| Chinese | 1 (4.5%) |  | 1 (9.1%) |
| Unknown or not reported | 0 |  |  |
| **Race** | American Indian/Alaska Native | 0 |  |  | 1 |
| Asian | 1 (4.5%) |  | 1 (9.1%) |
| Black or African American | 0 |  |  |
| Native Hawaiian or Other Pacific Islander | 0 |  |  |
| White | 21 (95.5%) | 11 (100%) | 10 (90.9%) |
| More than one race | 0 |  |  |
| Unknown or not reported | 0 |  |  |
|  |  |  |  |  |  |
| **Age (yr)** | Mean | 13.18 | 13.18 | 13.18 | 1 |
| Median | 13 | 13 | 13 |  |
| Standard Deviation | 2.34 | 2.32 | 2.48 |  |
| Minimum | 10 | 10 | 10 |  |
| Maximum | 17 | 17 | 17 |  |

\* Group Difference was determined by Fisher’s Exact test for categorical variables and t-test for continuous variables.

Section 2. Safety Assessments for All Participants

The AE data are available for 22 participants as of 7/28/2017. The following statistics were based on the AE data obtained from those 22 participants randomized to treatment groups. Participants had 3.6 events on average with SD= 2.62. Five participants haven’t reported any AE events up to date.

### Table 4. Incidence of Adverse Events by Standardized AE Category

| **Standardized AE Category** | **Total N=Subjects\*** | **Total %\*\*** | **Total N=Events\*\*\*** |
| --- | --- | --- | --- |
| Aggression | 1 | 4.5 | 1 |
| Anxiety | 2 | 9.1 | 2 |
| Decreased Appetite | 3 | 13.6 | 3 |
| Diarrhea | 3 | 13.6 | 4# |
| Dizziness | 1 | 4.5 | 1 |
| Drowsiness | 1 | 4.5 | 1 |
| Dry Mouth | 1 | 4.5 | 1 |
| Ear Infection | 1 | 4.5 | 1 |
| Elevated Bilirubin | 1 | 4.5 | 1 |
| Emotional Lability | 1 | 4.5 | 1 |
| Epistaxis | 1 | 4.5 | 1 |
| Eye Infection | 1 | 4.5 | 2# |
| Fatigue | 1 | 4.5 | 1 |
| Fever | 1 | 4.5 | 2# |
| Gastrointestinal issues | 2 | 9.1 | 2 |
| Headache | 3 | 13.6 | 3 |
| Hyperactivity | 1 | 4.5 | 1 |
| Insomnia | 1 | 4.5 | 1 |
| Irritability | 2 | 9.1 | 3# |
| Itchiness | 2 | 9.1 | 3# |
| Obsessive compulsive behavior | 1 | 4.5 | 1 |
| Rash | 2 | 9.1 | 2 |
| Sedation | 1 | 4.5 | 1 |
| Self-injurious behavior | 1 | 4.5 | 1 |
| Sinus Infection | 1 | 4.5 | 1 |
| Skin Infection | 2 | 9.1 | 3# |
| Sleep Disturbance | 2 | 9.1 | 2 |
| Sprain | 1 | 4.5 | 1 |
| Upper Respiratory Infection | 11 | 50 | 13# |
| Vomiting | 1 | 4.5 | 1 |
| Weight loss | 1 | 4.5 | 1 |

*\* Number of participants experiencing an adverse event (participant is to be counted only once for each adverse event)*

*\*\* % of total number of participants with AE data available to date (total N=22) in the study*

*\*\*\* Total number of events overall*

*# Indicate recurrence of same adverse event*

### Table 5. Incidence of Adverse Events by Standardized AE Category,

### Stratified by Treatment Group

|  | **Group A (n=11)** | | | **Group B (n=11)** | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Standardized AE Category** | **Total N= Subjects\*** | **Total %\*\*** | **Total N= Events\*\*\*** | **Total N= Subjects\*** | **Total %\*\*** | **Total N= Events\*\*\*** |
| Aggression | 1 | 9.1 | 1 | 0 |  | 0 |
| Anxiety | 1 | 9.1 | 1 | 1 | 9.1 | 1 |
| Decreased Appetite | 0 |  | 0 | 3 | 27.3 | 3 |
| Diarrhea | 1 | 9.1 | 1 | 2 | 18.2 | 3# |
| Dizziness | 0 |  | 0 | 1 | 9.1 | 1 |
| Drowsiness | 1 | 9.1 | 1 | 0 |  | 0 |
| Dry Mouth | 0 |  | 0 | 1 | 9.1 | 1 |
| Ear Infection | 0 |  | 0 | 1 | 9.1 | 1 |
| Elevated Bilirubin | 0 |  | 0 | 1 | 9.1 | 1 |
| Emotional Lability | 0 |  | 0 | 1 | 9.1 | 1 |
| Epistaxis | 0 |  | 0 | 1 | 9.1 | 1 |
| Eye Infection | 0 |  | 0 | 1 | 9.1 | 2# |
| Fatigue | 0 |  | 0 | 1 | 9.1 | 1 |
| Fever | 1 | 9.1 | 2# | 0 |  | 0 |
| Gastrointestinal issues | 0 |  | 0 | 2 | 18.2 | 2 |
| Headache | 1 | 9.1 | 1 | 2 | 18.2 | 2 |
| Hyperactivity | 1 | 9.1 | 1 | 0 |  | 0 |
| Insomnia | 0 |  | 0 | 1 | 9.1 | 1 |
| Irritability | 1 | 9.1 | 2# | 1 | 9.1 | 1 |
| Itchiness | 0 |  | 0 | 2 | 18.2 | 3# |
| Obsessive compulsive behavior | 0 |  | 0 | 1 | 9.1 | 1 |
| Rash | 1 | 9.1 | 1 | 1 | 9.1 | 1 |
| Sedation | 0 |  | 0 | 1 | 9.1 | 1 |
| Self-injurious behavior | 0 |  | 0 | 1 | 9.1 | 1 |
| Sinus Infection | 0 |  | 0 | 1 | 9.1 | 1 |
| Skin Infection | 1 | 9.1 | 2# | 1 | 9.1 | 1 |
| Sleep Disturbance | 1 | 9.1 | 1 | 1 | 9.1 | 1 |
| Sprain | 0 |  | 0 | 1 | 9.1 | 1 |
| Upper Respiratory Infection | 6 | 54.5 | 8# | 5 | 45.5 | 5 |
| Vomiting | 1 | 9.1 | 1 | 0 |  | 0 |
| Weight loss | 0 |  | 0 | 1 | 9.1 | 1 |

*\* Number of participants experiencing an adverse event (participant is to be counted only once for each adverse event)*

*\*\* % of total number of participants with AE data available to date (total N=11 per group) in the study*

*\*\*\* Total number of events overall*

*# Indicate recurrence of same adverse event*

### Table 6. Severity of Adverse Events by Treatment Group

|  | **Total Number of Participants \* (%\*\*) with** | | | |  |
| --- | --- | --- | --- | --- | --- |
| **Treatment Group** | **NO AE** | **Mild Event** | **Moderate Event** | **Serious Event** | **Group Difference p-value** |
| **Overall** | 5 (22.7%) | 12 (54.6%) | 5 (22.7%) | 0 | 0.5135 |
| Group A | 3 | 7 | 1 | 0 |  |
| Group B | 2 | 5 | 4 | 0 |  |

*\* Number of* ***participants*** *experiencing a certain severity of an adverse event where each participant is counted only once at the highest level of severity for the event*

*\*\* % of participants experiencing a certain severity of an adverse event*

|  | **Total Number of Adverse Events\* (%\*\*)** | | |  |
| --- | --- | --- | --- | --- |
| **Treatment Group** | **Mild** | **Moderate** | **Serious** | **Group Difference p-value** |
| **Overall** | 52 (83.9%) | 10 (16.1%) | 0 | 0.7313 |
| Group A | 20 | 3 | 0 |  |
| Group B | 32 | 7 | 0 |  |

*\* Total number of* ***events*** *experiencing a certain severity of an adverse event*

*\*\* % of events experiencing a certain severity of an adverse event*

### Table 7. Severity of Adverse Events by Standardized AE category

|  | **Group A (n=11)** | | | **Group B (n=11)** | | |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Total Number of Adverse Events by severity\*** | | | | | |
| **Standardized AE Category** | **Mild** | **Moderate** | **Total** | **Mild** | **Moderate** | **Total** |
| Aggression |  | 1 | 1 |  |  |  |
| Anxiety | 1 |  | 1 | 1 |  | 1 |
| Decreased\_Appetite |  |  |  | 2 | 1 | 3 |
| Diarrhea | 1 |  | 1 | 3 |  | 3 |
| Dizziness |  |  |  |  | 1 | 1 |
| Drowsiness | 1 |  | 1 |  |  |  |
| Dry\_Mouth |  |  |  | 1 |  | 1 |
| Ear\_infection |  |  |  | 1 |  | 1 |
| Elevated\_Bilirubin |  |  |  | 1 |  | 1 |
| Emotional\_Lability |  |  |  | 1 |  | 1 |
| Epistaxis |  |  |  | 1 |  | 1 |
| Eye\_Infection |  |  |  | 2 |  | 2 |
| Fatigue |  |  |  | 1 |  | 1 |
| Fever | 2 |  | 2 |  |  |  |
| Gastrointestinal\_issues |  |  |  | 2 |  | 2 |
| Headache | 1 |  | 1 | 1 | 1 | 2 |
| Hyperactivity | 1 |  | 1 |  |  |  |
| Insomnia |  |  |  | 1 |  | 1 |
| Irritability |  | 2 | 2 | 1 |  | 1 |
| Itchiness |  |  |  | 2 | 1 | 3 |
| Obsessive compulsive beh |  |  |  |  | 1 | 1 |
| Rash | 1 |  | 1 | 1 |  | 1 |
| Sedation |  |  |  | 1 |  | 1 |
| Self-injurious\_behavior |  |  |  | 1 |  | 1 |
| Sinus\_Infection |  |  |  | 1 |  | 1 |
| Skin\_Infection | 2 |  | 2 | 1 |  | 1 |
| Sleep\_Disturbance | 1 |  | 1 | 1 |  | 1 |
| Sprain |  |  |  |  | 1 | 1 |
| Up\_Respiratory\_Infection | 8 |  | 8 | 5 |  | 5 |
| Vomiting | 1 |  | 1 |  |  |  |
| Weight\_Loss |  |  |  |  | 1 | 1 |

*\* Number of events experiencing a certain severity of a given adverse event*

### 

### Appendix

### Listing 1: Adverse Events \*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Participant ID** | **Adverse Event** | **Severity** | **Frequency** | **Action Taken** | **Outcome\*\*** | **Relationship to Study Medication\*\*\*** |
| 30-01 | URI with congestion | mild | continuous | none | recovered | not\_related |
| 30-01 | Vomiting due to flu | mild | continuous | none | recovered | not\_related |
| 30-01 | Rash for 1 wk on right upper leg and back | mild | continuous | none | recovered | not\_related |
| 30-02 | Nosebleed | mild | single | none | recovered | not\_related |
| 30-02 | Dry mouth | mild | continuous | none | recovered | possibly\_related\_Less50 |
| 30-02 | Dizzy | moderate | intermittent | none | recovered | possibly\_related\_Less50 |
| 30-02 | Headache | moderate | intermittent | none | recovered | possibly\_related\_Less50 |
| 30-02 | Left conjunctivitis | mild | continuous | none | recovered | Unlikely |
| 30-02 | Eye redness | mild | intermittent | none | recovered | Unlikely |
| 30-02 | Decrease of appetite | moderate | continuous | concomitant\_med | recovering | possibly\_related\_Less50 |
| 30-02 | Cold | mild | single | none | recovered | Unlikely |
| 30-02 | Weight loss | moderate | continuous | none | recovering | Unlikely |
| 30-02 | Increase bilirubin from baseline and visit 2 | mild | continuous | none | recovering | Unlikely |
| 30-03 | Fatigue | mild | intermittent | none | recovered | possibly\_related\_Less50 |
| 30-03 | Emotional | mild | intermittent | none | recovered | possibly\_related\_Less50 |
| 30-03 | Constipation | mild | single | none | recovered | possibly\_related\_Less50 |
| 30-03 | Increased anxiety with dental visit | mild | single | none | recovered | not\_related |
| 30-03 | URI | mild | continuous | none | recovered | not\_related |
| 30-03 | Otitis Media | mild | continuous | none | recovered | not\_related |
| 30-03 | Sinusitis | mild | continuous | none | recovered | not\_related |
| 30-03 | Impetigo | mild | continuous | none | recovered | not\_related |
| 30-03 | Difficulty going to sleep due to not being in own bed | mild | single | concomitant\_med | recovered | not\_related |
| 30-04 | No AE Data During Study |  |  |  |  |  |
| 30-05 | Sedation | mild | continuous | dose\_decrease | recovered | probably\_related\_More50 |
| 30-05 | URI | mild | continuous | none | recovered | not\_related |
| 30-05 | Diarrhea | mild | intermittent | none | recovered | not\_related |
| 30-05 | Diarrhea | mild | single | concomitant\_med | recovered | Unlikely |
| 30-06 | Screen Fail No AE Data |  |  |  |  |  |
| 30-07 | Increase in hyperactivity | mild | continuous | concomitant\_med | unknown | possibly\_related\_Less50 |
| 30-07 | Sleep disturbance | mild | continuous | concomitant\_med and dose\_decrease | recovered | possibly\_related\_Less50 |
| 30-08 | Headache | mild | intermittent | concomitant\_med | recovered | possibly\_related\_Less50 |
| 30-08 | Fever | mild | intermittent | concomitant\_med | recovered | Unlikely |
| 30-08 | Fever | mild | intermittent | concomitant\_med | recovered | Unlikely |
| 30-09 | Nasal Congestion, Cough | mild | intermittent | none | recovered | Unlikely |
| 30-09 | Upper Respiratory Infection | mild | intermittent | none | unknown | Unlikely |
| 30-09 | Ingrown toenail s/p procedure to remove infection | mild | intermittent | none | recovered | not\_related |
| 30-09 | Finger infection | mild | intermittent | none | recovered | not\_related |
| 30-10 | URI Symptoms (fever, runny nose) | mild | intermittent | none | recovered | not\_related |
| 30-10 | Diarrhea | mild | intermittent | none | recovered | Unlikely |
| 30-11 | Itching | mild | intermittent | none | recovered | possibly\_related\_Less50 |
| 30-11 | Loss of appetite compared to baseline | mild | intermittent | none | recovered | possibly\_related\_Less50 |
| 30-11 | Itching occasional | mild | intermittent | none | recovered | possibly\_related\_Less50 |
| 30-11 | Rash on face | mild | intermittent | none | recovered | possibly\_related\_Less50 |
| 30-12 | Itching at wrists | moderate | intermittent | concomitant\_med | not\_recovered | possibly\_related\_Less50 |
| 30-13 | Nasal Congestion | mild | continuous | none | recovered | Unlikely |
| 30-13 | Headache | mild | single | concomitant\_med | recovered | Unlikely |
| 30-13 | Diarrhea (not water loss) | mild | continuous | none | recovered | possibly\_related\_Less50 |
| 30-13 | Sprained right elbow (xray no fracture so splinted) | moderate | single | concomitant\_med | recovered | not\_related |
| 30-13 | Constipation | mild | intermittent | concomitant\_med | recovered | Unlikely |
| 30-14 | Hitting nose with hand when frustrated or angry (has done before) | mild | intermittent | none | recovering | possibly\_related\_Less50 |
| 30-14 | Flu | mild | continuous | concomitant\_med | recovered | not\_related |
| 30-15 | No AE Data During Study |  |  |  |  |  |
| 30-16 | Sinus infection | mild | continuous | concomitant\_med | recovered | not\_related |
| 30-17 | URI | mild | continuous | none | recovered | not\_related |
| 30-17 | More jumpy and anxious | mild | continuous | none | recovered | possibly\_related\_Less50 |
| 30-17 | Continued irritability | moderate | continuous | dose\_decrease | recovering | possibly\_related\_Less50 |
| 30-17 | URI | mild | continuous | none | recovered | not\_related |
| 30-17 | Increase in irritability | moderate | continuous | drug\_permanently\_discontinued | recovering | possibly\_related\_Less50 |
| 30-17 | Aggresion | moderate | continuous | drug\_permanently\_discontinued | not\_recovered | probably\_related\_More50 |
| 30-18 | Nail picking obcessively with bleeding | moderate | continuous | dose\_decrease | recovering | probably\_related\_More50 |
| 30-18 | More irritable | mild | continuous | dose\_decrease | recovering | probably\_related\_More50 |
| 30-18 | Up at 5am | mild | intermittent | dose\_decrease | recovered | probably\_related\_More50 |
| 30-19 | Nasal Drainage Congestion | mild | intermittent | concomitant\_med | recovered | not\_related |
| 30-19 | Sleepiness | mild | intermittent | none | ongoing | possibly\_related\_Less50 |
| 30-20 | No AE Data to Report |  |  |  |  |  |
| 30-21 | No AE Data to Report |  |  |  |  |  |
| 30-22 | Decrease of appetite | mild | intermittent | none | recovered | Unlikely |
| 30-23 | No AE Data to Report |  |  |  |  |  |

*\* This listing was sorted by Participant ID.*

*\*\* Outcome: recovered, recovering,* not\_recovered, *ongoing,unknown*

*\*\*\* Unlikely, not related, possibly related <50% or >50%*