

September 10, 2017

Re: LB390 Annual Report

Dear Chairs of Judiciary and Health & Human Services Committees,

On the behalf of the University of Nebraska Medical Center and Deepak Madhavan, MD, we respectfully submit the 2017 annual report for the Cannabidiol Pilot Study. This study allows access to cannabidiol oil for patients who suffer from intractable or treatment-resistant seizures. The catalyst for the study was LB390 introduced by Senator Sue Crawford.

We would like to take this opportunity to present the current state of the Cannabidiol Study and provide you with an update regarding the study based upon data collected by the research team, including reports from the participants and families helping us to evaluate the use of cannabidiol oil.

Currently there are:

- 24 patients enrolled in the trial with 23 taking study drug
 - 11 patients under the age of 19
 - 2 patients recently withdrew from the study due to:
 - Elevated liver enzymes
 - Parents concerns of possible worsening seizures
- 23 currently on study drug
 - 13 are having good results in seizure control
 - 8 are seeing moderate improvements
 - 2 have seen minimal results
- Common adverse side effects have included sleepiness, unsteady gait, lethargy and a drop in the platelet count. These have generally resolved with adjusting the dosage of the study drug and/or their other seizure medications.

We were approved to receive cannabidiol from GW Pharmaceuticals sufficient to treat 25 patients. The two patients that withdrew from the study are being replaced, per agreement with GW Pharmaceuticals to provide drug for those additional patients. One was already replaced and an additional patient is expected to be consented in the next week. There were a total of 74 records submitted for initial consideration, and following screening of those that met criteria to participate and wanted to enroll, there remain 4 patients who expressed an initial interest in participating and meet initial criteria that we have not had adequate supplies to bring in to screen. If we are given the opportunity and study drug to do so, we will invite them to screen for the study also.

In terms of seizure frequency, it can be safe to say that we have not noticed worsening of seizure frequency from the drug. In some cases, there does not appear to be much of an affect at all. This is

likely dependent on the patient's epilepsy type, and also the other medications they are concomitantly taking. It may be that cannabidiol exerts part of its effect due to its interactions with other medications.

With regards to dosing, we have noticed the most effect correlated with a dose of 10-20 mg/kg/day. Once patients we have treated got to the 25 mg/kg/day dose, generally the side effects they experiences seemed to increase, without associated seizure prevention benefit. We have had to lower the dose on a number of these individuals. Additionally, in some cases were able to decrease the dosage on other seizure medications in combination with cannabidiol to reach a dosage that provided improved therapeutic results. It must be noted that these are observations based upon a small number of patients however, so generalizations must be tempered based upon the size of the study and the open-label approach.

A routine DEA audit occurred August 29, 2017 with the focus area being the research pharmacy. That visit went well, finding proper documentation in place and no findings from the DEA.

We greatly appreciate the support provided for this study on behalf of those Nebraska residents living with this chronic and debilitating condition.

Respectfully Submitted;

A handwritten signature in black ink, appearing to read 'Chris Kratochvil', written in a cursive style.

Christopher J. Kratochvil, M.D.
Associate Vice Chancellor for Clinical Research, UNMC
Vice President for Research, Nebraska Medicine