UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

GILDA HAGAN-BROWN,	)	
	)	
Plaintiff,	)	
	)	
-v-	)	CAUSE NO.
	)	1:14-CV-01614-AJT-JFA
	)	
ELI LILLY AND COMPANY, AN INDIANA CORPORATION,	)	
	)	
Defendant.	)	
and		
JANINE ALI,	)	
	)	
Plaintiff,	)	
	)	
-v-	)	CAUSE NO.
	)	1:14-CV-01615-AJT-JFA
	)	
ELI LILLY AND COMPANY, AN INDIANA CORPORATION,	)	
	)	
Defendant.	)	

The videotaped 30(b)(6) deposition upon oral examination of MADELAINE M. WOHLREICH, a witness produced and sworn before me, Michele K. Gustafson, CRR-RPR, Notary Public in and for the County of Marion, State of Indiana, taken on behalf of the Plaintiffs at the offices of Ice Miller, One American Square, 29th Floor, Indianapolis, Indiana, on April 30, 2015, at 10:08 a.m., pursuant to the Federal Rules of Civil Procedure.

APPEARANCES

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ALSO PRESENT: Brian Taylor, Videographer
Stephanie Tartaglia, Esq.
Michael Lynch, Esq. (by telephone)
Whitney Butcher, Esq. (by telephone)

Q Doctor, I've handed you what has been marked as Exhibit 6. I -- I don't know if this is the final protocol or the clinical study report, but this appears to be a document that identifies itself as the protocol for study HMBU; is that correct?
A That is -- says protocol for HMBU(a), yes.
Q Okay. And this was approved based on the first page on December 3, 2002?
A Protocol was approved December 3, 2002.
Q And the amended protocol was approved on 26th of February, 2003?
A Yes.
Q This study -- and if you want to look through it to answer this question, that's fine. But this study appears to be a head to head clinical trial comparing Cymbalta to Effexor; correct?
A Yes. That's my recall of this study.
Q Did you review this study before your deposition today?
A With -- with the attorneys, no.
Q Oh, just in -- just did you review the study at all before?
A No.
Q Okay.
A No, but I remember it --

Q Sure.
A -- by name. I was not personally involved with it, but was aware of it.
Q Dr. Perahia played a significant role designing the study, didn't he?
MR. STEKLOFF: Object to form.
A I don't know that. I would believe it. He was -- he was in the global team at the time this study was done, but I'm not sure what his role was in this.
Q And one of the reasons -- now, if you look at the clinical trial, let's go to the diagram of the actual trial setup. Find that page for you. I think it's on page 23.
A Yes.
Q Bates number ending in 4175. It appears that there's one, two, three, four study periods. Do you see that?
A Yes.
Q And the fourth study period has its own diagram. That appears to be a taper period?
A Yes.
Q And it looks like -- well, can you explain to me what the tapering regimen that's described here for the various treatment arms?

A It's fairly complicated based on which drug the patients were on and also what dose they were on. And there's a different taper -- slightly different taper schedule two for duloxetine, one for patients who were on 90 and 120 milligrams in which they were tapered -- it doesn't give the weeks but over several study visits. And then one for patients who were on 60 of duloxetine, one for patients who were taking 225 of venlafaxine and one for patients taking 75 and 150 milligrams daily of venlafaxine. And I presume the final one is placebo or is that continuation. It's a little bit difficult for me to understand what that last seven plus one day is.

Q Okay. And if you -- it appears if you -- if the patient was taking 90 or 120 milligrams of duloxetine between the end of Period III and visit 301, they were reduced to 60 milligrams a day?

A For a week, I presume.

Q For -- yeah, looks to be about a week.

A Yeah. Actually it's not clear from this, but for a period of time.

Q Yeah. Between --

A 60, then 30, then 0 amount of duloxetine.

Q Thank you.

A Uh-huh.

Q And if you were taking 60 milligrams a day duloxetine, you went down to 30, then to placebo, and then to no study drug?
A Right.
Q Okay. And if you were taking venlafaxine, which is the chemical name for Effexor; right?
A Effexor is a brand name --
Q Yeah.
A -- for venlafaxine, yes.
Q If you were taking 225 milligrams, you were reduced to 150 milligrams, then 75, then nothing?
A Then no study drug.
Q Then no study drug.
A (The witness nodded.)
Q And then if you were at 75 or 50 -- 150 milligrams of venlafaxine, it went to 75 for the first period, placebo, and then nothing; is that right?
A Correct, and I now understand that the seven plus or minus a day is the duration of those three intervals of taper.
Q So it appears that there's a -- either a taper of two to three -- one-, two-, or three-step taper off of the drug spanning from one to 21 days?
MR. STEKLOFF: Object to form.
Q Or is that mathematically off?

A Not quite.
Q Okay.
A It's a one or two-week taper followed by a week on no study drug.
Q Okay. Do you know who designed this taper period?
A I do not.
Q Would it surprise you if it was Dr. Perahia?
MR. STEKLOFF: Object to form.
A No. He was on the global team, and I believe he had a prominent role in this study.
Q Okay.
(Exhibit 7 was marked for identification.)
MR. WISNER: This has been covered with the sticker.
MR. STEKLOFF: That's fine.
MR. WISNER: Did I just hand you two?
MR. STEKLOFF: No.
Q All right, Doctor. I've handed you -- this is an e-mail exchange. It's Bates stamped CYM-01780901 through CYM-01780905. And this is a series of e-mail exchanges. I do not believe you were copied on any of these e-mails.
A Looks like not.
Q Okay. Have you ever seen this e-mail exchange before?

this is -- this appears to be the results from the HMBU half of the study?

A From the HMBU half of data that was intended and by advanced plan and protocol to be analyzed together.

Q Okay. Great. And if you look at the next exhibit, this is a table, and it says Treatment-Emergent Adverse Events collected by AMDP-5. Do you know what that is?

A I'm not sure.

Q Okay. It says by decreasing frequency -- if you want to look at the protocol, by the way.

A The protocol is probably not going to be helpful. Or if I need to look at the protocol for one of your questions, I'll let you know. Is that all right?

Q Sure. If you just look at page 19 on the protocol or end in Bates stamp 171. It's in objectives section.

A Yes.

Q No association for methodology and documentation in psychiatry, and it says AMDP-5.

A I'm sorry. You're --

Q I'm sorry. I'm in the first paragraph under primary objective.

A Okay.

Q It just says --
A Yes.
Q If you read down there, it says, Risk is defined by four categories. It says, No association for methodology and documentation in psychiatry, AMDP-5. Do you see that?
A Yes.
Q So be fair to say that the AMDP-5 is referring to the association for methodology and documentation in psychiatry?
A I would -- I would assume that to be true.
Q Do you know what that is?
A I really don't.
Q Okay. Do you -- do you know if it's a checklist that's used to evaluate symptoms?
A I don't.
Q Okay. Well, it says here Treatment-Emergent Adverse Events collected by -- and by the way, here, I believe we're on Exhibit 9?
A Yes.
Q Page 686, you see that?
A Uh-huh.
Q And it says, Treatment-Emergent Adverse Events Collected by AMDP-5 By Decreasing Frequency, All Patients who Entered Study Period --

significant?

MR. STEKLOFF: Object to form.

A I don't think that's quite right, but . . .

Q Fair enough.

A I don't think your math is quite right.

Q And it'd be fair to say here, then, that the difference observed base on this AMDP-5, which we don't know what that is, but that the patients with at least one TESS for duloxetine and venlafaxine are not statistically different -- statistically significantly different?

MR. STEKLOFF: Object to form.

A On this page, yes.

Q Okay. You said that there was a companion study done for this -- with this?

A Yes.

Q And that was HMCQ; right?

A Correct.

(Exhibit 10 was marked for identification.)

Q All right. Doctor, I've marked a document that's been labeled Exhibit 10. This is a table and it reads, Treatment-Emergent Adverse Events Collected by AMDP-5 -- AMDP-5 By Decreasing Frequency, All Patients who Entered Study Period IV. And it has HMCQ Study Period IV. You see that?

A Yes.
Q So this appears to be the equivalent table to Exhibit 8 that we looked at a second ago?
A It's equivalent for study HMCQ to the one we looked at for BU.
Q And in this one patients with at least one TESS under duloxetine at 74.1 percent and venlafaxine is 81.2 percent?
A That's correct.
Q And, again, the p-value is not statistically significant?
A For patients who had at least one adverse event, there is no difference in this -- in this part of the two-part study.
Q And, in fact, if you just quickly look through the p-values here, the only -- there doesn't appear to be any -- any --
A No. There are several that are statistically significant if you look at the p-value column.
Q Okay. So diarrhea, for example, is different?
A Yes, diarrhea's one.
Q And then --
A Vomiting. Or is it -- I'm sorry. It's very small print.
Q I understand.

there was 44.6 percent greater than or equal to -- sorry. There was 44.6 percent of patients experienced at least one TESS on duloxetine and 55.2 percent experienced at least one TESS on venlafaxine; is that right?

A Yes.

Q And is that a statistically significant value?

A No. P-value is .159.

Q Okay. So it would be fair to say, then, that at least based on the studies that I've shown you -- actually scratch that, Doctor.

Based on your understanding of the data measuring discontinuation-emergent events, whether it be in a taper or an abrupt fashion, in the clinical trials that Lilly has conducted, it has not shown that there is a statistically significant difference between the overall risks -- let me -- scratch that question. Let me rephrase that again.

Doctor, does the clinical data that Lilly possesses regarding comparing venlafaxine to Cymbalta with regards to discontinuation-emergent adverse effects show that there's an overall difference for the number of patients who experience at least one discontinuation-emergent adverse event in its clinical data?

A If you're talking about the total number of adverse events, it does not show a difference. But some of the individual adverse events show a statistically significant difference.
Q Sure. And --
A So the overall take on that to me as a physician and a scientist would be to suggest that there may be some difference.
Q Okay. But isn't it true, Doctor, that -- one second, Doctor.
A When looking --
Q Doctor, I have no pending question, please. One second.
MR. STEKLOFF: That's fine.
THE WITNESS: Okay.
Q Okay. I have no further questions, Doctor, on that document.
A Okay. All right.
Q Are you aware of any other clinical trials where Lilly directly compared Cymbalta to venlafaxine?
A I'm not.
Q Okay. Lilly also conducted studies to measure the difference between -- pardon me. Lilly also conducted studies to measure the difference of discontinuation-emergent adverse events compared to

abruptly stopping Cymbalta as opposed to tapering off the medication; right?

MR. STEKLOFF: Object to the form.

A I believe it did in at least one of its studies.

(Exhibit 13 was marked for identification.)

Q Doctor, I have handed you what I've marked as Exhibit -- the court reporter's marked as Exhibit 13. This is a study -- well, it says on the top HMBR study report. See that?

A Yes.

Q And it begins with the Bates number CYM-00745626; right?

A Yes.

MR. STEKLOFF: 262.

MR. WISNER: Let me say that again.

Q It starts with CYM-00745262; is that right?

A Yes.

Q Okay. And this is a study -- well, please turn the page over and look at page 34. I represent to you these are selections of pages from the study report. Okay? I didn't provide the whole thing. So if you look at page 1 on the top was in the front page, and if you turn the page the second page is actually page 34. You see that?

A Yes.

Q Okay. And this is the section labeled Investigational Plan?
A Yes.
Q All right. And if you look down here at the diagram of the study design, this is an example of a clinical trial where in the Study Period IV there was a tapering and abrupt discontinuation of Cymbalta; correct?
A I'm sorry. I don't see that from the study diagram. I would have to read it. Okay. Yes. At the bottom of the diagram it says, Half of the patients in the duloxetine 60 milligrams QD, which means daily, and duloxetine 120 milligrams daily treatment groups started on placebo immediately following visit 8, whereas the other half of patients in these treatment groups tapered off duloxetine.
Q Okay. So this is an example of the study design -- the study -- the types of study that I was talking about a second ago?
A Yes.
Q Okay. And this was for the GAD indication?
A Generalized anxiety disorder, GAD.
Q That was going to be my next question. And this was a registry clinical trial; right?

A That's my understanding.
Q And by registry clinical trial, this was one that was going to be compared in support of a regulatory application to market the drug for the specific indication?
A It's a study done for a regulatory body in order to achieve approval.
Q Turn to -- one second, Doctor. Okay, Doctor. If you could turn to at the -- page number of the document is 145 but it's actually the Bates stamp ending 406. Do you see that?
A Yes.
Q Okay. This is a table and it says, Discontinuation ad -- Emergent Adverse Events, Preferred Term by Decreasing Frequency, Logistical Regression Analysis -- I'm sorry -- Logistic Regression Analysis. You see that?
A Yes.
Q Do you know what a logistic regression analysis is?
A I could not define that for you.
Q Okay. It reads here, All Duloxetine Patients Enter Drug-Tapering Phase, Drug-Tapering Phase. You see that?
A Yes.
Q All right. And then it lists four different

groups; right? The first group is duloxetine 60 milligrams a day abrupt; right?

A Yes.

Q And the second one is 60 milligrams duloxetine taper; right?

A Yes.

Q And then there's two more groups also for abrupt and taper for 120 milligrams a day; right?

A Yes.

Q Okay. And if you look at the results here, at least in the first line of this, patients with one or more discontinuation-emergent events, the -- for the 60 milligrams abrupt, it says 31 percent; right?

A Yes.

Q And for the 60 milligram taper, it says 31.3 percent?

A Yes.

Q And for the 120 milligrams a day abrupt, that's 36.2 percent?

A Yes.

Q And then for the 120 milligrams taper, that's 24.2 percent?

A Yes.

Q And the p-value is .83; right?

A Yes.
Q And that's -- that's not statistically significant?
A I'm not sure what that p-value refers to because there are four groups.
Q If you look down at the bottom, it says, Frequencies are analyzed using logistic regression with treatment, stopping method and treatment times stopping method in the model. Does that help you understand that or not at all?
A I'm afraid not.
Q Okay. Well, the p-value represented on this chart does not show any statistical significance; correct?
A That's not a statistically significant p-value.
Q And --
A But I'm not sure what's being compared.
Q And these percentages, 31 -- these percentages that I just read back to you, it would appear that there's no statistically significant difference between them due to the lack of variability?
MR. STEKLOFF: Object to form.
A All I see is a p-value. I have no idea what it means or what it refers to.
Q Well, isn't it true that in this study that Lilly conducted, there was no statistically significant

difference between the percentage of individuals who experience at least one discontinuation-emergent adverse event regardless of whether they tapered or they abruptly stopped the medication?

A I can't verify that because I really don't understand a p-value in logistic regression analysis.

Q That is your understanding independent of this table; correct?

A My understanding is that a p-value of .83 is not statistically significant, but I'm not sure what's being compared by this p-value.

Q I appreciate your answer. Maybe my question wasn't clear. It is your understanding -- putting this document aside, it was your understanding before you looked at it today that there was no statistically significant difference shown in the GAD study between abrupt and taper; correct?

A I don't recall. I'd have to -- if you show me a study report or some summary -- is that what we just saw?

Q Yes. If you just go to the page before.

A Yes.

Q Just says Table H -- bottom paragraph -- sorry,

Doctor. It's the one ending Bates number 405.
A Okay.
Q It's the page just before the table. Do you see that?
A Okay.
Q And it says, Display of Adverse Events.
A There was no statistical difference among the study groups, okay.
Q Do you see that?
A Tapered and abrupt. Yes. Thank you.
Q So that's correct? There was no statistical significance between the study groups between the taper and abrupt; right?
A Okay. That I understand.
Q Okay. Are you aware of any other studies that Lilly has done to measure the difference between abrupt or taper discontinuation from Cymbalta?
A Not that I recall.
Q Okay. Do you recall if -- so you don't recall any other studies that might have measured that?
A No.
Q All right.
VIDEOGRAPHER TAYLOR: Five minutes on tape.
MR. WISNER: Let's switch the tape.
VIDEOGRAPHER TAYLOR: 3:05. We are off the

THE REPORTER: Okay. When would you like to have them by?

MR. WISNER: I'd like to have them all by next Friday.

THE REPORTER: Okay.

MS. TARTAGLIA: You can send it to all four attorneys and to myself. I'll e-mail you with the particulars.

THE REPORTER: Thank you.

(The deposition concluded at 3:34 p.m.)

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-v-	)	CAUSE NO. 1:14-CV-01614-AJT-JFA
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and		
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ELI LILLY AND COMPANY, AN INDIANA CORPORATION, Defendants.	)	

Job No. 97563

I, MADELAINE M. WOHLREICH, state that I have read the foregoing transcript of the testimony given by me at my 30(b)(6) deposition on April 30, 2015, and that said transcript constitutes a true and correct record of the testimony given by me at said deposition except as I have so indicated on the errata sheets provided herein.

_____
MADELAINE M. WOHLREICH