UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

HELSINN HEALTHCARE, S.A. and ROCHE PALO ALTO, LLC,

Plaintiffs,

-vs-

DR. REDDY'S LABORATORIES, LTD., DR. REDDY'S LABORATORIES, INC., TEVA PHARMACEUTICALS USA, INC., and TEVA PHARMACEUTICAL INDUSTRIES, LTD.

Defendants.

CIVIL ACTION NUMBER:

11-3962

TRIAL

WITH SEALED PORTIONS

Clarkson S. Fisher United States Courthouse
402 East State Street
Trenton, New Jersey 08608
June 15, 2015

B E F O R E: THE HONORABLE MARY L. COOPER
UNITED STATES DISTRICT JUDGE

Certified as True and Correct as required by Title 28, U.S.C., Section 753

/S/ Regina A. Berenato-Tell, CCR, CRR, RMR, RPR
/S/ Carol Farrell, CCR, CRR, RMR, CCP, RPR, RSA

United States District Court
Trenton, New Jersey

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I N D E X

(In open court. June 15, 2015, 9:30 a.m.)

THE COURT: Good morning, everyone.

ALL: Good morning, your Honor.

THE COURT: How is everybody today?

ALL: Good.

THE COURT: Okay. What would you like to start with this morning?

MR. ASHKENAZI: Your Honor, we're planning on playing some deposition designations this morning.

THE COURT: All right. Is there any dispute about them, these?

MR. ASHKENAZI: Not that I'm aware of.

MR. SENDER: Other than the sort of the standing 403 objection to our experts who did not appear, you know, we've designated what we could out of it to try to provide some context.

THE COURT: All right. Well, I'll see them, and I'll rule at some point. But we'll definitely know what we're delineating as your objection.

MR. SENDER: Thank you, your Honor.

MR. LIZZA: Your Honor, in that regard as requested by your Honor for the line-by-line analysis, we've prepared a chart with the designations and with our basis for relevance and probative value. So if I may approach, I can hand that chart up.

THE COURT: Sure. Have you served it?

MR. SENDER: No, they have not, your Honor.

MR. LIZZA: We're serving it now.

THE COURT: Okay. And, again, you don't need to respond until you've had a chance to digest it and me, too. Okay? Fine.

MR. ASHKENAZI: Your Honor, at this time, we'd like to play the deposition designation of Dr. Maurie Markman who is DRL's expert clinical oncologist. According to DRL, Dr. Markman is the president of medicine and science at Cancer Treatment Centers of America. Dr. Markman has more than 20 years of experience in cancer treatment. He has held clinical, research, teaching and management positions in several highly regarded medical institutions in the U.S.

Dr. Markman has extensive experience with all the 5-HT_3 receptor antagonist drugs approved in the U.S. Dr. Markman was deposed regarding his expert opinions in this case.

And for the record, your Honor, we have a binder with the corresponding deposition exhibits. Markman Deposition Exhibit 1 corresponds to DTX-1206.

THE COURT: I'm sorry. Just a second, please. I'll tell you when I'm ready.

MR. ASHKENAZI: Okay.

THE COURT: Was he deposed once or twice?

THE COURT: Okay. I'm just reviewing what you've already told me.

What is this institution where he practices? President of medicine and science at the organization called Cancer Treatment Centers of America. This is a whole consortium of hospitals? Where does he practice?

MR. ASHKENAZI: Your Honor, that was the description provided to us about Dr. Markman. He's DRL's expert. I guess I would defer to them on what that institution is.

THE COURT: All right. Never mind.

Thank you. So, what were you saying?

MR. ASHKENAZI: Just providing for the record which DTXs correspond to the deposition exhibits identified during the video.

So, Markman Deposition Exhibit 1 corresponds to DTX-1206. And, your Honor, this is in the binder under tabs. Markman Deposition Exhibit 1, Exhibit I is DTX-283. Markman Deposition Exhibit 4 is PTX-398, and Markman Deposition Exhibit 11 is PTX-297.

THE COURT: Okay. Will you be showing on the screen these exhibits, or is that going to be too cumbersome?

MR. ASHKENAZI: I believe we will be showing them on the screen, your Honor.

THE COURT: Okay.

MR. ASHKENAZI: Thank you.

THE COURT: Fine. And about how long is this video?

MR. ASHKENAZI: This one is 23 minutes, your Honor.

THE COURT: Okay. Fine.

(The video deposition of Maurie Markman was played as follows:)

Q. Dr. Markman, good morning.

A. Good morning.

Q. Let's take a look at your opening report, Exhibit 1, specifically Paragraph 4. It states here that you were asked by counsel for DRL to provide expert opinions on certain issues related to the clinical aspects of the asserted claims of the '219 patent, correct?

A. That's correct.

Q. Can you tell me generally what your experience is with respect to palonosetron, perhaps starting with any use of palonosetron you have in your clinics?

A. Well, it's a drug that I've used, you know, extensively since the day it was -- came on the market. I can't tell you, you know, the number of times. I treat patients with gynecological malignancies, that's my clinical expertise, and we use a lot of platinum, which is not only the drug that gave chemotherapy its bad name 20, 30 years ago, but it's also the drug that is the one -- from the point of view of nausea and vomiting, but it's also the drug that -- where -- the class of

So, I've used all of the serotonin antagonists, and this is -- obviously a wonderful product and used it -- I've used it extensively.

Q. Can you elaborate on what it is about Aloxi® that you think makes it a wonderful product?

A. Well, I -- you know, I think it's a -- you know, serotonin antagonists have been around for a long time. And they were -- when they first came into existence now many, many years ago, they changed the way we thought about the management of chemotherapy-induced emesis.

What Aloxi® -- I'll say Aloxi®, it's easier, shorter, the benefit of that drug was that it had a very important effect on -- we divide nausea and vomiting in chemotherapy at least with a highly emetogenic chemotherapy, like platinum, into what we call acute, and then we call it delayed emesis. And -- and what had been very well recognized is that the serotonin antagonists were quite effective and the -- that is, the first generation, again, I -- when I use the term "first generation," to be.

THE COURT: Just a second, I'm sorry. There's a transcription error back there, and I wouldn't want the court reporter here to not be informed about that transcription error in the dep.

If you'll just scroll back a moment. And I'm not going to pick up every one, but if I think that it's worth noting, I

will.

A. That drug was that it had a very important effect on -- we divide nausea and vomiting in chemotherapy at least with a highly emetogenic chemotherapy, like platinum, into what we call acute and we call delayed emesis.

THE COURT: Okay. Stop it. You see that word, "but" that he's about to reach? What he actually says is "what had been." "What had been very well recognized." I think you'll agree with me when you hear it.

THE WITNESS: Very well recognized --

THE COURT: Back it up. We missed it.

THE WITNESS: -- shorter, the benefit of that drug was that it had a very important effect on -- we divide nausea and vomiting in chemotherapy at least with a highly emetogenic chemotherapy, like platinum, into what we call acute and we call delayed emesis. And what had been very well recognized is that the serotonin antagonists were quite effective in the -- that is, the first --

THE COURT: "In the." "In the" not "and the."

THE WITNESS: But I'll use the term "first generation" to be ondansetron, granisetron were very effective in the acute nausea and prevention of acute nausea and vomiting, not perfect, but certainly a lot better than the existing standards at that time when they came on existence.

vomiting, and Aloxi® was the first drug of that category or actually any category that was effective both for acute and delayed. And, so, nausea and vomiting induced by highly emetogenic chemotherapy. So, with the introduction of this drug, it became, you know, widely utilized by oncologists, including me.

Q. So, just to make sure I have that, you mentioned that the Aloxi® was the first drug approved for delayed emesis in connection with highly emetogenic chemotherapy?

A. Well, the one thing I want to -- I mean, you know, I'm not 100 percent sure about who approved what, when or things like that, I'll tell you. From my perspective at a clinical level, their registration strategies and things get approved, but at a clinical level I think what I said is certainly correct, and it may actually registration true, too, I'm not -- I'm speaking at the clinical level.

Q. Would you agree that one of the benefits of Aloxi® versus the first generation of 5-HT_3s was its ability to treat delayed emesis associated with CINV generally?

A. Yes.

Q. So, you mentioned that you continue today to prescribe Aloxi®; is that correct?

A. Absolutely.

Q. And you started prescribing Aloxi® when it was first approved back in 2003?

A. If that was the date, yes.

Q. Not to be a memory test.

Have -- over the course of the last roughly, say, decade that you've been prescribing Aloxi®, have your -- the frequency of your prescriptions with respect to Aloxi® changed at all during that time period?

A. I would say I don't -- I don't think so.

Q. Do you prescribe other antiemetics in connection with your practice?

A. I do. And I would certainly -- I think it's appropriate to add when you go back to your previous question and, I'm sorry, I should have answered you know some of the determinations are made today by a contracting issues and, you know, this is a market, there are other opportunities and there are other approaches towards management of acute and delayed emesis. And, so, some of those decisions are actually made, I don't want to say at a higher level than me, but a different level than me.

Q. For example, I would imagine that given the presence of -- or the availability of generic 5-HT_3s that at times I would assume you prescribed generic?

A. Well, I would say that's certainly one approach. And the other approach is, of course, there are the use of generics and the other categories of drugs that could prevent delayed

Q. NK-1 receptor antagonists?

A. Right.

Q. So, I'm asking about that POSA standard you've applied, this hypothetical person, would that hypothetical POSA, in deciding what drug molecule to pursue for development, take into account the sort of market considerations we have been discussing?

A. I believe so.

Q. Do you have an opinion as yes or no what standards you applied in this case whether a POSA would take those generic competition and number of competitor products into account in deciding whether to pursue a drug product or not?

A. I believe they probably would, yes.

Q. So, we've done a little bit of this already, so I'll try not to be duplicative, but I want to talk about the state of the art in antiemetics in 2002.

So, that's the time period that's relevant to your opinions in this case. Roughly 2002, 2003, correct?

A. Correct.

Q. So, is it correct that in this time period you were obviously a practicing clinician, correct?

A. Correct.

Q. And I assume that you studied the literature and remained up to date on developments in the field at that time?

A. That's correct.

Q. You were comfortable providing opinions about what the state of the art at that time was, correct?

A. That's correct.

Q. And did you stay up to date on potential new therapies under development in the antiemetic field?

A. Um, yes.

Q. And did that include potential new therapies that would treat CINV, for example?

A. That's correct.

Q. And I think you said this before, but, please, I don't want to put words in your mouth, so correct me if I'm wrong, but I think you essentially said that the 5-HT_3 antagonists that were available in 2002 weren't -- weren't -- weren't satisfactory in terms of treating delayed CINV; is that correct?

A. I believe that was the -- it would be a fair statement of my opinion, as well as that of what the clinical community would -- would say, as well.

Q. Was it also true in 2002 that the available setrons were comparable in effectiveness and toxicity?

A. The serotonin antagonist inhibitors, yes.

Q. Then available?

A. Yes.

Q. Would you also agree that in the 2002 time period,

control?

A. Well, you know, again, it's a -- it -- your -- it's a little hard to answer that question. I mean, you could say today we're not perfect either. I think we -- what -- what happened with the availability of the serotonin antagonists, there was a tremendous improvement, and certainly with the acute nausea and vomiting, and it became the delayed that was a greater concern, but even then we still had a, as we do now, still a percentage of patients where at least they would say the therapies are not as good as we'd like them to do.

So, it's a -- I think it's a relative answer. I would certainly have said then, and I'll say now, we're not perfect. We have gotten better, but, you know, if you look at 2002, 2003 compared to ten years earlier before the availability of the serotonin antagonists, we were much better. It's you know, again, it is all relative.

Q. It would be helpful if you could get Tab 7. It's very convenient in fact that you wrote a paper in 2002 that I think touches upon a lot of this, so it is very convenient.

A. Thank you.

Q. Do you recognize this document, Exhibit 4?

A. Well, yes.

Q. Can you tell me what it is?

A. It's a review article I wrote for the Cleveland Clinic Journal of Medicine when I was at that institution in 2002.

Q. And does it sort of generally summarize the paper is discussing essentially the state of the art in the treatment of CINV in the 2002 time period?

A. I haven't looked at this for a long time, but I -- I certainly would have every reason to believe that that is exactly what this paper does.

Q. Okay. So, for example, on the first page, we were just talking about on the right side column, it's about midway down the page you see there's a sentence that starts, "Given the complexity of"...

A. Yes.

Q. All right. If you could just -- well, I'll read it into is the record. "Given the complexity of the emetic process and the multiple neuroreceptors involved, chemotherapy-induced emesis has been extremely difficult to control completely."

Do you see that?

A. Yes.

Q. And do you agree that that was consistent with the state of the art in 2002 concerning antiemetics?

A. Yes.

Q. All right. You state here, "For example, an antiemetic agent that completely inhibits a specific neuroreceptor involved in emesis may activate another receptor that leads to nausea and vomiting by an alternative pathway," correct?

Q. Do you agree with that statement, as well, in terms of the state of the art in antiemetics in 2002?

A. Yes.

Q. And the paragraph continues, "Furthermore, although the neurophysiology of acute emesis is fairly well characterized, our understanding is extremely limited of the pathways involved with either delayed or anticipatory nausea and vomiting."

Do you see that?

A. Yes.

Q. Is that also in your opinion an accurate view of the state of the art of antiemetics in 2002?

A. Yes.

Q. If you can turn next to Page 612. And I'm interested in the text that is underneath the heading delayed emesis. Do you see that, the left side?

A. Yes.

Q. It states, "Unfortunately, the pathophysiology and neuropharmacology of delayed emesis are poorly understood."

Do you see that?

A. Yes.

Q. And do you agree that also accurately reflects the state of the art of antiemetics in 2002?

A. Yes.

Q. Is it correct that it was known in 2002 that the

pathophysiologic processes of delayed and acute emesis differed?

A. Well, what we knew is that if a patient had, you know, very good control or fairly good control, it didn't --

THE COURT: All right. Let's back it up to where he begins his answer. This word "pathophysiology" is kind of a new one.

Q. Is it correct it was known in 2002 that the pathophysiologic processes of delayed and acute emesis differed?

A. Well, what we knew is that if a patient had, you know, very good control or fairly good control, it didn't -- of acute, it didn't -- it didn't necessarily translate into a control of delayed. That's what we knew.

Q. So, you knew the mechanisms between acute and delayed were different?

A. Well, again, we -- what we knew is was the clinical outcome was different, and --

Q. Okay.

A. And whether, you know, this was the entirely different process or somehow we weren't adequately controlling the acute process, again, we -- we didn't know the mechanism, still don't know the mechanism. We have hypotheses of the mechanisms and we have much better therapies, but, certainly,

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