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trospium chloride patients (after an average of 14.3 days.) Do you see that?

A I do, yes.

Q Are those -- are with -- is withdrawal an important consideration in whether or not an overactive bladder drug is efficacious?

MS. WOOTEN: Objection, form.

A It doesn't have anything to do with efficaciousness, but it has to do with tolerability of the patient. So it's a very important issue.

BY MR. OELKE:

Q I should say -- yeah, I'm sorry, I should say effective, whether it's an effective OAB treatment?

A Again, and it can be effective, but the patients can't tolerate it, so they stop taking it.

Q Okay.

A And that's -- that's the case with oxybutynin.

Q Okay. Now, for most OAB patients that are put on -- on drugs, how long does it -- does it take for the patient to get the -- the desired effect from the drug?

A It's extraordinarily variable.

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Q Okay.

A And it can be as quickly as a few days, but most often it's several weeks before they have the maximum effect.

One has to realize that when you do a study of any of the overactive bladder drugs, there's a significant placebo effect for many patients.

As many as 30 percent of patients will have some placebo response. So you could give them a Vitamin B and about a third of them would feel better. So it's a little hard to tease that out.

But -- but generally it takes several weeks for them to have a maximum effect.

Q And an OAB drug is -- will only get approved if it shows an efficacy over placebo, though, right?

A That's correct.

MR. OELKE: Let's mark as 9, an article entitled Characterization of Darifenacin as a Novel Radioligand for the Study of Muscarinic M3 Receptors by Carolyn Smith and Rob Wallis.

(Deposition Exhibit 9 marked.)

THE WITNESS: Thank you.

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BY MR. OELKE:

Q Have you seen Carson 9 before?

A I have not.

Q Okay.

A Not that I know of. I mean, it's a long time ago, so I may have but I don't think so.

Q Okay. So I don't think we need to spend too much time on it then.

But you recognize it's an article concerning darifenacin?

A Yes.

Q And it's dated 1997?

A Correct.

Q So at least as of 1997, darifenacin was being studied as a selective M3 inhibitor, right?

A Yes.

Q And there were other compounds also being studied for selective M3 inhibition, right?

A Yes.

Q And why was selective M3 inhibition being studied as a -- as a possible lead for OAB drugs in the 1998-1999 time frame?

MS. WOOTEN: Objection, form.

A In the bladder, the predominant

muscarinic receptors are M2, which has the largest number. M3, second largest number. But M3 is the most functionally responsible receptor, so it's the one that you'd want to target.

Unfortunately, M3 is also present in the salivary glands and in the gut. So even being selective doesn't necessarily eliminate all of those side effects.

But if you could just target a clean drug that was only effective on M3, then you have a higher chance of affecting the overactive bladder with diminished side effects.

BY MR. OELKE:

Q And was darifenacin successful in reducing adverse side effects?

A To an extent. The trouble with darifenacin is the bioavailability was variable.

So at this -- you know, if it was really very well bioavailable, it would have changed the -- changed the landscape of overactive bladder treatment, but it just wasn't or isn't.

Q So in 1998, would a reasonable path for research by OAB researchers to make a more bioavailable version of darifenacin?

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MS. WOOTEN: Objection, form.

A Certainly would have been a thought.

BY MR. OELKE:

Q Okay. And it would have been a reasonable path, right?

A Yes.

MS. WOOTEN: Objection, form.

BY MR. OELKE:

Q And solifenacin, was it successful as a M3 selective inhibitor?

A Also similar to darifenacin, selective, yes, but bioavailable not so much -- not as -- not as much as one would like.

Q Okay. And is constipation a prominent side effect for those -- those two compounds?

A For many patients, yes.

Q So would a reasonable approach have been to try to make a -- to start with darifenacin or solifenacin and make it -- make it compounded that had fewer side effects with respect to constipation?

MS. WOOTEN: Objection, form.

A I mean, that would be a thought, but because there's M3 receptors in the bowel, it would

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be a little hard to separate the bladder and the bowel and the three receptors. So if you're going to affect one, you're going to affect the other.

BY MR. OELKE:

Q But there's M3 receptors in salivary glands, too, right?

A Yes, that's correct.

Q Did darifenacin or solifenacin show a benefit with respect to dry mouth?

A Well, they all had dry mouth and dry eyes, so, a benefit, no. A complication or a side effect, yes.

Q Okay.

MR. OELKE: I would like to mark as Carson Exhibit 10, Abstracts of Paper -- well, it's -- I'll just give the Bates numbers, two pages. MYLB_FESO-0027337 to 0338.

(Deposition Exhibit 10 marked.)

THE WITNESS: Thank you.

BY MR. OELKE:

Q This is an abstract from April of 1997. Do you see that?

A Yes.

Q It was presented at the American Chemical

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Society National Meeting?

A Right.

Q And if you look at the abstract that's 046. Do you see that?

A Yes.

Q It's entitled 1,2,3,4-tetrahydro-2-isoquinolinecarboxylate derivatives.

MR. OELKE: Sorry about that.

A Yes.

BY MR. OELKE:

Q A Novel Class of Selective Muscarinic Antagonists. Do you see that?

A Yes.

Q And the first named author is Takeuchi?

A Yes.

Q And that's -- they were at Yamanouchi Pharmaceutical, right?

A Right.

Q And Yamanouchi is the company that developed solifenacin?

A Uh-huh, yes.

Q And do you understand this abstract concerns solifenacin?

A No, but -- I don't know the chemical name for solifenacin to be honest.

Q Okay. It's my understanding this is an early abstract that concerns solifenacin.

A Okay.

Q Now, if you look in that -- in that paragraph in the abstract, five lines down, it says, Among those compounds, and then it lists that same compound.

A Okay.

Q I won't -- I won't write it out, but it's a -- I won't read it out, but it's YM-53705 is the shorthand for it. Do you see that?

A Yes.

Q It said, It showed high affinity for M3 receptor and a Ki value; is that right?

A That's what it says.

Q Of 12 nano -- of 12nm and 10-fold selectivity between rhythmic contraction and salivary secretion. Do you see that?

A Yes.

Q So does this indicate that -- that M3 selectivity is -- is between or at least they had tested it for between an effect on the bladder

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and -- and the salivary?

A Yes.

Q Okay. And their conclusion is that YM-53705 will be expected as a drug for the treatment of urinary incontinence without side effects such as dry mouth.

A Yes.

Q Do you see that?

It's kind of a hopeful statement there?

A Yes.

Q Okay. But at least there -- there's an indication that the dry mouth would be less?

A Would be less, right.

MR. OELKE: I would like to mark as Carson 11 an article entitled Anti-muscarinic Potency and Bladder Selectivity of PNU-200577, a Major Metabolite of Tolterodine.

(Deposition Exhibit 11 marked.)

THE WITNESS: Thanks.

BY MR. OELKE:

Q Do you recognize Carson Exhibit 11 as an article by Dr. Nilvebrant and others?

A Yes.

Q Do you understand Dr. Nilvebrant was one

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of the inventors of tolterodine?

A Yes.

Q Do you know Dr. Nilvebrant?

A I do not.

Q Now, do you understand that PNU-200577 is another term that's used for 5-HMT?

A Yes.

Q Okay. And if you look at the abstract of this article, four lines up from the bottom, it says: Thus, PNU-200577 is similar to tolterodine in terms of anti-muscarinic potency, functional selectivity for the urinary bladder in vivo and absence of selectivity for muscarinic receptor subtypes in vitro. Do you see that?

A Yes.

Q So the conclusion of Dr. Nilvebrant, based on these studies, is that tolterodine and -- and 5-HMT are similar in terms of anti-muscarinic potency, right?

A Yes.

Q And -- and similar in their terms of their functional selectivity in vivo, right?

A Yes.

Q Now, Dr. Nilvebrant conducted studies

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in -- in cats, right?

A Yes.

Q And some of that is discussed here?

A I think this was not cats, though.

Q If you look at the in vivo results.

A It was guinea pigs as well, so...

Q Right, there is in vitro studies in guinea pigs.

A Yeah.

Q But if you look on Page 170, it says, In Vivo Studies. It says: The anti-muscarinic effects of PNU-200577 in vivo were studied in the anesthetized --

A Oh, right.

Q -- anesthetized cat. Right?

A Correct. Yeah. They also used bladder strips from the guinea pigs, so they did both --

Q Right.

A -- both things, in vivo and in vitro.

Q Are you familiar with these -- these anesthetized cat studies?

A I'm familiar with them, I've never done one.

Q Okay. If you look in the Discussion

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section of this article on Page 171.

It says: In the anesthetized -- did I say that right? -- cat, PNU-200577 produced a dose-dependent inhibition of acetylcholine-induced urinary bladder contraction and electrically stimulated salivation, and was almost three times more potent for inhibition of urinary bladder contractions compared with salivation. Right?

A Yes.

Q So these studies established or at least suggested that the tolterodine metabolite was more active in the bladder than in the salivary gland, right?

A That's what --

MS. WOOTEN: Objection, form.

A That's what it's suggesting. Whether that translates into a clinical advantage or not I guess remains to be seen based on this.

BY MR. OELKE:

Q Right.

It's not necessary that what's seen in cats is going to translate to humans, for instance?

A Correct.

Q Okay. If you look at the last paragraph

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in this -- in this article, it says: In summary, the pharmacological in vitro and in vivo profiles of PNU-200577 are almost identical to those of tolterodine, the parent compound. Do you see that?

A Yes.

Q So, again, this is supporting the concept that extensive metabolizers and poor metabolizers are going to end up getting the same net effect from the administration of tolterodine orally, right?

MS. WOOTEN: Objection, form.

A I'm not sure that you can totally say that because, again, of the -- because of the protein binding issues. I think that -- that has -- certainly has an effect on the effect in -- in patients and humans. But as far as in a laboratory setting, the two are equivalent.

BY MR. OELKE:

Q Okay.

MR. OELKE: I would like to mark as Carson 12 an article entitled Influence of CYP2D6 polymorphism on the pharmacokinetics and pharmacodynamics of tolterodine. First author Niclas Brynne.

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(Deposition Exhibit 12 marked.)

THE WITNESS: Thank you.

BY MR. OELKE:

Q Have you seen the Brynne article before, Dr. Carson?

A Yes, I have.

Q The -- the objective of this study was to determine whether 2D6 is involved in the metabolism of tolterodine, right?

A Yes.

Q And also to investigate potential differences of tolterodine in 5-HMT between poor and extensive metabolizers, right?

A Correct.

Q And the conclusion of the study is that, if you look there in the abstract, it says: Tolterodine is extensively metabolized by -- by CYP2D6 with high specificity. Despite the effect on pharmacokinetics, the CYP2D6 polymorphism does not appear to be of great importance in the anti-muscarinic effect, probably because of the additive action of parent drug and the active metabolite. Right?

A Yes.

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Q So the -- the authors of this article, including Niclas Brynne, was that tolterodine and 5-HMT had an additive action, right?

A Yes.

Q And that poor metabolizers and extensive metabolizers receive the same net effect?

A In this study, that's correct.

Q And this was a study that was specific to tolterodine, right?

A Yes, it was.

Q So the conclusion of both the Brynne article, the Nilvebrant -- so the conclusion of the Nilvebrant article which was Carson Exhibit 11 --

A Uh-huh.

Q -- the Brynne article which is Carson Exhibit 12, and the label for Detrol, which is Carson Exhibit 7, is that the net activity for poor metabolizers and extensive metabolizers is the same, right?

A Yes.

Q Okay.

MR. OELKE: I would like to mark as Carson Exhibit 13 a document entitled Tolterodine, A new muscarinic receptor antagonist, is

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metabolized by cytochromes P450 2D6 and 3A in human liver microsomes, by Postlind and others.

(Deposition Exhibit 13 marked.)

THE WITNESS: Thank you.

BY MR. OELKE:

Q Have you seen Carson Exhibit 13?

A Yes, I have.

Q And this is a study in human liver microsomes for tolterodine?

A Yes.

Q And the conclusion that's stated in the abstract is: We conclude from these studies -- this is the last sentence -- We conclude from these studies that the formation of 5-HM -- and you understand that 5-HM, is 5-HMT, right?

A Yes.

Q That the formation of 5-HM is -- is catalyzed by CYP2D6 and that the formation of N-dealkylated tolterodine is predominantly catalyzed by CYP3A isoenzymes in human liver microsomes. Right?

A Yes.

Q Now, in your report, your opening report you cite to the Postlind article, right?

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A I do, yes.

Q If you look at Page 18.

A Okay.

Q On Page 18 you cite to a paragraph that's on Page 292 of Postlind, so it's at the end.

Now, the last paragraph of Postlind starts: Clinical studies have demonstrated that individuals with reduced CYP2D6-mediated metabolism represent a high-risk group in the population with a propensity to develop adverse drug effects. Right?

A Yes.

Q And it cites to Smith 1986.

And you state in your report that this paragraph, in Paragraph 63, you say: This information is important to a clinician because it helps to inform the risks associated with dosing tolterodine. Right?

A Yes.

Q Now, this statement -- first of all, Postlind didn't study, did he, the net activity of tolterodine in 5-HMT, right, in humans?

MS. WOOTEN: Objection, form.

A Can you say that again? I'm not quite

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sure about that.

BY MR. OELKE:

Q This Postlind article isn't --

A Yeah.

Q -- about the activity of tolterodine in 5-HMT in humans when it's dosed orally, is it?

A No, it's not.

MS. WOOTEN: Objection, form.

BY MR. OELKE:

Q It's about liver microzymes, right?

A Right.

Q Microsomes, sorry.

And it does not have any conclusion in it about whether there are certain risks associated with poor metabolizers for the administration of tolterodine orally to patients, right?

A Well, I mean, basically he does say in his discussion that, you know, clinical studies have demonstrated that individuals with reduced or poor metabolizers represent a high risk group in the -- in the population with a propensity to develop adverse drug effects. So he states that in his --

Q Right.

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A -- in his discussion, right.

Q But that statement is citing to Smith in 1986, right?

A Yes.

Q Smith 1986 doesn't have anything to do with tolterodine, does it?

A But it has to do with cytochrome 2D6.

Q Right.

A And that basically has something to do with tolterodine as well, right, so...

Q But 1986, when Smith was written, tolterodine hadn't even been invented yet, right?

A It hadn't, but cytochrome P450 2D6 had been identified and --

Q Right.

A -- was being studied and had been studied.

Q Right.

And Smith is talking about other drugs, not tolterodine, right?

A That's correct. He's talking about other drugs, but he's talking about that enzyme system.

Q Right. But we've also established that there were studies that were done specifically on

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tolterodine, right?

A Correct.

Q And those studies, which we just looked at, Brynne, Nilvebrant and also it's in the label, they all come to the conclusion that the net effect is the same for poor metabolizers and extensive metabolizers, right?

A Yes.

MS. WOOTEN: Objection, form.

BY MR. OELKE:

Q So this concern that's discussed here in Smith was found not to be applicable to tolterodine and 5-HMT, right?

A In the studies that are reported, that's correct, the ones we've talked about.

Q Okay.

MR. OELKE: Let's take a break.

VIDEO TECHNICIAN: Going off the record.

(Recess taken 11:26 a.m.)

VIDEO TECHNICIAN: Back on the record, 11:43.

BY MR. OELKE:

Q Now, in 1998-1999, there were no long-acting OAB drugs on the market, right?

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A That's correct, they were all multiple day dosing.

Q Okay. And at some point once daily drugs did become available, right?

A Yes, they did.

Q Okay. And when was that?

A Roughly 2001.

Q Okay.

MR. OELKE: I would like to mark as Exhibit 14 an article, Fesoterodine is an effective anti-muscarinic for patients with overactive bladder (OAB): Results of a Phase 2 Trial by Nitti, et al.

(Deposition Exhibit 14 marked.)

THE WITNESS: Thank you.

BY MR. OELKE:

Q Have you seen this article, Dr. Carson?

A I have, yes.

Q Okay. And this is a study of fesoterodine, right?

A Yes, that's correct.

Q And they tested 4, 8 and 12 milligram doses of fesoterodine once daily?

A Yes.

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Q Okay. And placebo, right?

A Yes.

Q And if you look at the Concluding Message which is on the second page: Determined that All 3 doses of fesoterodine led to significant and clinically relevant improvements from baseline in several parameters, e.g., frequency, urge incontinence and voided volume per micturition. Right?

A Yes.

Q Okay. And so do you recall when fesoterodine was first introduced into the market?

A I think it was in the 2004 range.

Q Okay. And what would -- did you at that time prescribe fesoterodine to patients?

A Yes.

Q Okay. And what was your clinical experience with fesoterodine?

A It was good. I had no -- you know, they all work some and they all have side effects in some and some patients respond better to one than another, so -- but generally it was good.

Q Okay. And it's -- it's approved at 4 milligrams and at 8 milligrams, right?

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A That's correct.

Q Okay. And so were there some patients that you prescribed 8 milligrams of fesoterodine to?

A Yes.

Q And were some of those patients that you had tried dosing tolterodine?

A Yes.

Q Okay. And why did you switch those patients from tolterodine to fesoterodine?

A Couple of reasons. No. 1 is, it's a newer drug, so you always want to try something different.

No. 2 thing is, is that there were purportedly fewer side effects.

No. 3 thing is, is that there are actually a couple of studies that looked at head-to-head experience between tolterodine max dose and fesoterodine max dose, and it showed that the maximum dose of fesoterodine was more effective.

And finally, that, you know, there -- there were, again, active marketing of the drug, so we wanted to try new things. And as an academic

urologist, I feel it's my responsibility or part of it to try the latest drugs.

Q So these -- these head-to-head studies of 8 milligrams of fesoterodine to 4 milligrams of tolterodine, those studies were of the -- the maximum dose approved for each of those drugs, right?

A Maximum approved dose, yeah. I mean, whether you could actually compare the doses or not is a matter of dispute, but those are the maximum-approved doses.

Just like when we talked about the oxybutynin study, it was the maximum approved doses of each of the -- each of the agents.

Q So it's a very common thing when you're doing a head-to-head study to compare a maximum-approved dose of each drug?

A In -- in -- in post marketing trials, it's almost always done that way.

Q Okay. But going back to the Nitti article, his conclusion is that for all of these different doses, 4, 8 and 12, they actually tested 12 milligrams here as well, that they led to significant and clinically relevant improvements

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for the parameters they tested which were frequency, urge incontinence and voided volume per micturition, right?

A Yes.

Q Okay. And those are all important parameters, correct?

A That's what you're trying to really treat. That's what the patients are bothered by.

Q Okay. And he also concluded that improvements were seen as early as two weeks after randomization. Do you see that?

A Yes.

Q Was that a benefit of fesoterodine that it showed early improvement?

MS. WOOTEN: Objection, form.

A There are -- there are studies that show that it was quicker -- a quicker onset than some of the ones that were already on -- on the market, yes.

BY MR. OELKE:

Q All right. And that -- was that a surprising result for fesoterodine?

A Not so much. I -- you know, it -- it was one of those things that most of the other drugs

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didn't have those trials, rapidity of onset trials.

So some of the -- some of the trials that are done are done for marketing purposes and that was a marketing trial in my opinion.

Q Okay.

MR. OELKE: I would like to mark Carson Exhibit 15, an article entitled Role of Pharmacokinetics and Metabolism in Drug Discovery and Development by Lin and Lu, production numbers PFE01847326 to 372.

(Deposition Exhibit 15 marked.)

THE WITNESS: Thanks.

BY MR. OELKE:

Q Have you seen this article before?

A I have not.

Q Okay.

A Not that I know of. Looks interesting, though.

Q Just give me a second.

If you look in your opening report of the materials considered.

A Okay.

Q I think if you look at -- it's on --

A Got it, Exhibit 2.

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Q Table of exhibits. If you look at the table of exhibits at the front of the --

A Yeah.

Q The front.

A I guess I have seen this, yeah.

Q Yeah, I think if you look at Paragraph 33, you cite to it.

A Yeah, yeah, I did see this.

Q Okay. And it's an article that discusses metabolism in drug development, right?

A Yes.

Q And drug discovery.

And if you look at -- there's a section that starts at Page 436.

A Okay.

Q Which is PFE01847359.

A Right.

Q And that section's called Pharmacogenetics of Drug Metabolism.

A Yes.

Q If you look at the end of -- it gives a number of examples, but if you look at the end of that section on Page 439, the last paragraph. It says there: As described above, genetic

polymorphism in drug metabolism is undesirable and can at times be problematic.

Excuse me.

Do you see that?

A Yes.

Q What does polymorphism refer to there?

A Basically differences in the ability of a patient to metabolize drugs. The -- the high metabolizers of -- and -- and nonmetabolizers of D2 -- of 2D6 are examples of that polymorphism.

Q Okay.

A Some patients do, some patients don't.

Q It goes on to say: However, it should be emphasized that even if a large proportion of the metabolism of a compound is subject to genetic polymorphism, this should not influence its development as a drug. Do you see that?

A Yes.

Q Careful evaluation of clinical relevance of polymorphic metabolism has to be taken into consideration in making the go/no-go decisions. Right?

A Yes, uh-huh.

Q So with respect to tolterodine, that

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careful evaluation of clinical relevance is described in -- in the Nilvebrant and Brynne article and the Detrol label, right?

A It is, yes.

Q They took a look at whether polymorphism was a problem for tolterodine, right?

A They did.

MS. WOOTEN: Objection, form.

BY MR. OELKE:

Q And the conclusion that they drew was that the net activity for tolterodine and 5-HMT was the same, right?

MS. WOOTEN: Objection, form.

A They showed there was an effect, but overall clinical effect was -- was minimal.

BY MR. OELKE:

Q Right. The overall difference in clinical effect --

A Exactly.

Q -- was minimal, right?

And so with respect to the example of tolterodine -- in fact, the genetic polymorphism turned out not to be undesirable with respect to tolterodine, right?

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MS. WOOTEN: Objection, form.

A I wouldn't say that. I wouldn't make that strong a statement, but I would say that -- that in a -- in a clinical experience it really didn't make a difference as far as the clinical outcomes are concerned.

BY MR. OELKE:

Q Okay. You can set that aside.

MR. OELKE: I think let's take a break now. It will be easier.

VIDEO TECHNICIAN: Marks the end of Video 2. Off the record, 11:57.

(Lunch recess.)

* * * * *

VIDEO TECHNICIAN: Marks the beginning of Video 3. Deposition Culley Carson, M.D. Back on the record. Time 12:52.

BY MR. OELKE:

Q Good afternoon, Dr. Carson.

A Good afternoon.

MR. OELKE: I would like to mark as

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Carson Exhibit 16 an article entitled Superiority of Fesoterodine 8-milligram versus 4-milligram in reducing urgency urinary incontinence episodes in patients with overactive bladder: results of the randomized, double-blind, placebo-controlled EIGHT trial with Chapple, et al. as authors. Bates range is PFE01843522 to 530.

(Deposition Exhibit 16 marked.)

THE WITNESS: Thanks.

BY MR. OELKE:

Q Have you seen Carson Exhibit 16 before?

A Yes, I have.

Q And are you familiar with Chris Chapple?

A Yes, very familiar. I know him personally.

Q Okay. And is he a urologist?

A Yes, he is.

Q Is he a well-respected urologist?

A Very much so.

Q Okay. And this is a study concerning 8 milligrams versus 4 milligrams of fesoterodine, right?

A Yes, it is.

Q And if you look at the conclusions, it

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states there: In a 12-week, prospectively-designed, superiority trial, fesoterodine 8 milligrams showed statistically significantly superior efficacy versus fesoterodine 4 milligram and placebo, as measured by reductions in UUI episodes and other diary variables, diary-dry dry rate, and improvements in measurement -- measures of symptoms -- symptom bother, HRQL, and other PROs. Do you see that?

A Yes.

Q And it says: Clear evidence of dose-dependent efficacy is unique to fesoterodine among anti-muscarinics and other oral agents for treatment of OAB. Do you see that?

A Yes.

Q So is it your understanding that prior to this trial, no other OAB treatment had been shown to have dose dependent efficacy?

A There were other trials that look at different doses and showed different outcomes, so -- but this showed a -- you know, if you raise it this much, then you raise the effects by the same amounts.

Q Okay. And prior to this study, there had

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never been a demonstration of such a dose-dependent efficacy relationship in a -- a designed -- prospectively-designed trial, right?

A Correct.

MS. WOOTEN: Objection, form.

A Okay. This trial was designed to show that particular thing. Other trials were basically subgroup analyses and post hoc analyses of -- of other -- of larger trials.

BY MR. OELKE:

Q Are you aware of any other OAB drug that has shown dose-dependent efficacy effect?

MS. WOOTEN: Objection, form.

A Well, they all do better at the higher dose than they do at the lower dose, and, you know, that's been demonstrated in a lot of studies.

But as far as showing -- showing it as -- as specifically as this, this is the only trial that I'm aware of that showed that re -- that result.

BY MR. OELKE:

Q Okay. Was that an important result for fesoterodine?

MS. WOOTEN: Objection, form.

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A I think it was -- yeah, I think it was important for the marketing of fesoterodine for sure.

BY MR. OELKE:

Q Well, was it important for -- not for the marketing of fesoterodine, but for -- in comparison to other OAB drugs, did it demonstrate something that was important to urologists?

MS. WOOTEN: Objection, form.

A That's a little hard to say because urologists always try to up dose patients if they're not responding well.

And we know that for patients on fesoterodine, about 50 percent of them are up dosed anyway in a -- as a clinical -- as a -- as a clinical reality.

And so at -- at the end of the day this showed what we all sort of already knew, I guess, is what I'm -- what I'm trying to get at.

BY MR. OELKE:

Q Did you ever tell Dr. Chapple that?

A Not that specific thing. I mean, I know Chris Chapple extremely well, but I -- I'm not sure that we talked about this particular paper

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together.

Q Okay. Dr. Chapple certainly didn't indicate that this was just a confirmation of what was already known about OAB drugs, did he?

MS. WOOTEN: Objection, form.

A Well, that's not what he was trying to show. He was trying to show that this was true with fesoterodine and he did show that.

BY MR. OELKE:

Q Right.

And it hadn't been shown for any other OAB drug prior to this?

A Not in this specific way.

Q Okay.

MR. OELKE: I would like to mark as Carson Exhibit 17 an article entitled Fesoterodine Dose Response in Subjects With Overactive Bladder Syndrome. And Vic Khullar is the first named author. PFE00574418 to 4422.

(Deposition Exhibit 17 marked.)

THE WITNESS: Thanks.

BY MR. OELKE:

Q Are you familiar with Carson Exhibit 17?

A Yes, I am.

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Q Are you familiar with this study?

A Yes.

Q And at the beginning of this -- so this study also concerns fesoterodine dose response, right?

A Yes, it does.

Q And are you familiar with any of these authors?

A Yes, several of them I know well personally.

Q Okay.

A Rovner, Dmochowski and Nitti.

Q Okay. And are those respected urologists?

A Yes.

Q Now, at the beginning of this article, it says: Many patients with overactive bladder syndrome are successfully managed with anti-muscarinic agents, but responses are variable.

Further therapeutic benefit might be achieved with higher doses; however, dose escalation has not become routine in clinical practice.

This may be, in part, because fixed-dosed

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studies with the anti-muscarinic agents darifenacin and solifenacin have failed to demonstrate clear efficacy dose-response in parallel dosing studies.

Do you see that?

A Yes.

Q So for some OAB drugs they had tried to make a dose escalation study that would -- that would demonstrate a clear efficacy dose response and they were -- they were unsuccessful, right?

A That's correct.

Q And those were darifenacin and solifenacin?

A Right, yes.

Q And so, in fact, when you say that fesoterodine as studied by Chapple was just -- on fesoterodine was just showing what everyone suspected, in fact, there had been other OAB drugs where, in fact, it wasn't shown, right?

MS. WOOTEN: Objection, form.

A There were some that were and some that weren't, so, correct.

BY MR. OELKE:

Q Well, some that were and some that weren't. What others besides fesoterodine have

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ever been shown to have a dose escalation response with respect to efficacy?

A Oxybutynin --

Q When was that?

A -- early on. Early on in their -- in their period of time they started with the 5 milligrams and then eventually got to 5 milligrams three times daily. So, you know, that was definitely well-known.

Q If you look at Page 842.

A Okay.

Q The second column there. If you would start with the third line in that second column. It says: Their dose separation has not been demonstrated for efficacy outcomes with darifenacin, solifenacin, or tolterodine. Do you see that?

A Yes.

Q So, in fact, tolterodine is another OAB drug for which dose separation couldn't be shown with efficacy outcomes, right?

A That's right.

MS. WOOTEN: Objection, form.

A And -- and let me just back up just a

little bit with that.

Because basically there was a definite differentiation between the two doses, but it was not statistically significantly different in the trials when they looked at the two different doses.

So you could say that it was different but statistically it was not different and probably clinically was not different.

BY MR. OELKE:

Q Right. And in fact, tolterodine, almost all patients are dosed at 4 milligrams, right?

A Start right off at the top, exactly.

Q So there's really not a dose escalation scheme with tolterodine by practicing physicians, right?

MS. WOOTEN: Objection, form.

A Well, generally for practicing physicians they start out with 4 milligrams. And then if the patient has good response and side effects, they back off to 2 milligrams. So rather than dose escalating they dose deescalate.

BY MR. OELKE:

Q Okay. So that was a real benefit of fesoterodine over tolterodine, wasn't it, that you

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could dose escalate for patients that needed dose escalation?

A Yes, absolutely.

Q Okay. And the -- the head-to-head studies of fesoterodine 8 milligrams versus 4 milligrams in tolterodine, those studies showed there was a real efficacy benefit for patients that took 8 milligrams of fesoterodine in comparison to patients that took 4 milligrams of tolterodine, right?

MS. WOOTEN: Objection, form.

A It was shown, but, and the big -- the capital B in that but is that I'm not sure. And in fact, I don't think that 4 milligrams and 8 milligrams are equivalent doses. That's No. 1.

But No. 2 thing is that the difference is, while statistically significant, were probably not clinically significant.

And the reason I say that is, is that if you look at -- I don't remember which one of the studies it is particularly, but there was a 0.1 incontinence time per week difference between the two, which was statistically significant. But I would argue that's not clinically significant to

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the patient.

So, yes, the -- the study did show statistical significance. Does that mean there's clinical significance between -- between those? Probably not.

BY MR. OELKE:

Q But you have had patients that you had dosed on 4 milligrams of tolterodine and when that -- were not successful on that dose, you switched them to 8 milligrams of fesoterodine, right?

A Yes. And Steve Kaplan did a very nice study showing that people that were failures on tolterodine, they were then treated with 8 milligrams of fesoterodine were rescued. So, yes.

But there were also patients that were successfully treated with 4 milligrams of tolterodine. So that's kind of the piece of that.

Q But there's certainly a group of patients for which fesoterodine does show a real clinical benefit over what's available on the market with tolterodine, right?

A Yes.

MS. WOOTEN: Objection, form.

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Just give me a chance to put the objections --

THE WITNESS: Oh, I'm sorry.

MS. WOOTEN: -- before you answer.

THE WITNESS: Sorry.

MR. OELKE: I would like to mark Carson Exhibit 18. An article entitled Efficacy and safety of fesoterodine 8 milligrams in subjects with overactive bladder after a suboptimal response to tolterodine ER by Kaplan, et al. Bates range PFE01844264 to 272.

(Deposition Exhibit 18 marked.)

BY MR. OELKE:

Q Dr. Carson, do you see Exhibit 18?

A Yes.

Q And you recognize this article?

A I do.

Q And is this the article that shows a benefit in patients who have a suboptimal response to tolterodine 4 milligrams a day being switched to 8 milligrams of fesoterodine?

A Yes.

Q Is this a well-designed study?

MS. WOOTEN: Objection, form.

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A Yes, it's a well-designed study, but it takes a subgroup of patients that -- that failed -- failed tolterodine, and there are many patients that do well with tolterodine.

But the question is, what do you do with those patients that don't respond to it? And this shows you have an option, and the option is the highest dose of fesoterodine.

BY MR. OELKE:

Q And would this be referred to as a nonresponder study?

A Yes.

Q Okay. And nonresponder studies are a -- an accepted clinical trial that's used to show the efficacy of a -- of a drug in comparison to another drug, right?

MS. WOOTEN: Objection, form.

A Yes.

BY MR. OELKE:

Q And this trial, in fact, does show the benefit of fesoterodine 8 milligrams for those patients who don't respond to 4 milligrams of tolterodine?

MS. WOOTEN: Objection, form.

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A It does, but I would argue -- or I would question that if you could raise the dose of tolterodine would you get the same response. And I don't know the answer to that nor does this study demonstrate that.

BY MR. OELKE:

Q Well, have you ever dosed tolterodine patients at 8 milligrams a day?

A I have.

Q Okay. And that's -- would be off label?

A It would be off label, yes.

Q Okay. Have you ever dosed them at higher than 8 milligrams?

A No.

Q Okay. Have you ever dosed patients at higher than 8 milligrams of fesoterodine?

A I have, yes.

Q Okay. And what dose have you dosed those patients?

A The max I've -- the maximum I've ever gone is -- is 12.

Q Okay. And do you have an understanding of why tolterodine's maximum dose is 4 milligrams?

A Well, in the studies they looked at

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different side effects, and the side effects of higher doses, and it was mostly in the 6- to 8-milligram range of tolterodine, had a significant prevalence, I guess, of -- of acute urinary retention.

There was also at very high doses the concern about QT abnormalities, QT prolongation. So a lot of the -- the side effects were magnified at those doses.

And so it's one of those things where the FDA kind of guides drug companies as to what dose they -- they will accept based on efficacy and adverse events.

Q Okay.

MR. OELKE: I would like to mark as Carson Exhibit 19 an article entitled Tolterodine - A new bladder selective muscarinic receptor antagonist: preclinical pharmacological and clinical data by Nilvebrant, et al. And the Bates is PFE01844667 to 674.

(Deposition Exhibit 19 marked.)

THE WITNESS: Thanks.

BY MR. OELKE:

Q Dr. Carson, have you seen Exhibit 19

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before?

A I have, yes.

Q Okay. If you would look at -- well, first of all, this -- this summarizes pharmacological -- I mean, preclinical pharmacological and also clinical data for tolterodine, right?

A Yes, it does.

Q And if you look at Page 1135 which is PFE01844673. And to be clear, it shows that on that page there's a table that shows the different doses that were -- were studied, right?

A Yes.

Q And its doses in milligrams bd?

A Yes.

Q So this was immediate release tolterodine?

A Correct.

Q And those different doses were 0.5, 1, 2 and 4 bd?

A Yes.

Q So the highest dose was 8 milligrams a day?

A Right.

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Q Okay. And below that table there's a paragraph that -- that starts out: Tolterodine was well-tolerated and the adverse events reported were mainly of an anti-muscarinic nature. Do you see that?

A Yes.

Q And then six lines down, it says: However, five cases of urinary retention occurred, four in the 4-milligram bd group and one in the 2-milligram bd group. Together with the market increase in residual volumes observed in the 4-milligram bd group, this indicates that a dosage of 4-milligrams bd is too high. Do you see that?

A Yes, I do.

Q So Dr. Nilvebrant and -- and her co-authors concluded that 8 milligrams a day of tolterodine was too high, right?

A Yes.

Q And that urinary retention was a big reason for that, right?

A Was a risk.

Q Okay.

A Was a higher risk at that dose than at lower dose, although, the lower dose risk was not

zero.

Q Right, right.

Now urinary retention, is that a serious effect to be concerned about when you dose patients?

A Oh, absolutely. That -- that's one of the -- one of the things you fear about these drugs and one of the reasons that they weren't used in men for many years, that the conventional wisdom was, that if you used an anti-muscarinic in a male, that they would go into urinary retention.

Q Okay. And you understand that fesoterodine at 8 milligrams, that the -- the -- the risk of urinary retention is very minimal?

A I do.

MS. WOOTEN: Objection, form.

BY MR. OELKE:

Q It's like 1 percent?

A It's -- it's 1 percent, yeah. And that's pretty much what it is for all the other drugs, too. And that's what -- that's one of the ways that they establish what the maximum dose is.

Q Okay. And so wasn't it a surprising result that fesoterodine that acts with the same

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active metabolite as tolterodine would not have a urinary retention issue at 8 milligrams while tolterodine did?

MS. WOOTEN: Objection, form.

A Well, tolterodine acts in two ways, right? 5-HMT is one piece and then tolterodine itself is another piece. So you have basically two active forms of -- of drug that are acting on the bladder, right?

So, I mean, you have two things. And it's nicer to have actually a clean drug that just has one. The metabolite and the drug itself are the only thing that you're -- that you're titrating or treating with.

But in answer to your question there, because you have two it's hard to tease out which one of those is most responsible for the urinary retention.

BY MR. OELKE:

Q But the urinary retention was believed to be dose dependent, right?

A Oh, of course. And you can -- you can have urinary retention with fesoterodine if you dose it high enough, too.

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Any -- any of the anti-muscarinics, I don't care which one you choose, if you dose it high enough, you can completely paralyze the bladder -- the detrusor muscle.

Q Okay. But you're -- what you told me is that one of the reasons you need to be careful about comparing 8 milligrams of fesoterodine to 4 milligrams of tolterodine is, you think that they're getting the same -- you're not sure they're getting the same effect since there's twice as much fesoterodine being dosed as tolterodine.

Well, why wouldn't that same also apply to the side effect of urinary retention?

A Because you've got -- instead of one -- one moiety producing the physiological effect, you've got two. So the combination may effect -- does effect the bladder differently than the independent 5-HMT.

Q But as of 1998, there was no indication in the art that urinary retention was attributable to either 5-HMT or tolterodine, right?

MS. WOOTEN: Objection, form.

A This is true, but it was known that tolterodine did cause urinary retention.

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So if you could come up with a drug that relaxed the bladder better but had less risk of urinary retention, then, you know, that would be a -- that would be a home run.

BY MR. OELKE:

Q But there was nothing in the art as of 1998 that showed that you could take that urinary retention risk out by making a 5-HMT pro drug, was there?

A That wasn't available --

MS. WOOTEN: Objection, form.

A That was not available in the literature at that time.

BY MR. OELKE:

Q Okay. Now, as to the QT effect --

MR. OELKE: Mark another exhibit. Carson Exhibit 20. Thorough QT Study of the effect of fesoterodine on cardiac repolarization.

(Deposition Exhibit 20 marked.)

THE WITNESS: Thanks.

BY MR. OELKE:

Q Have you seen this article?

A Yes, I have.

Q Now, I know you mentioned it this

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morning, but can you again explain what the QT effect is?

A Sure. There's the Q wave, the R wave, the S wave in the -- in the cardiogram. The different -- the distance between the Q wave and the T wave are -- is measurable. And as it increases, it increases the risk of potentially fatal cardiac arrhythmias.

And so the FDA has a -- has a threshold of lengthening that they -- that they will not allow drugs to go beyond and still be approved.

Q Okay. And they studied in this paper the QT effect at both a 4-milligram dose of fesoterodine and a 28-milligram dose, right?

A Right.

Q And their conclusion was that both the 4- and 28-milligram dose did not show an increase with respect to the QT effect, right?

A That's correct.

MS. WOOTEN: Objection, form.

BY MR. OELKE:

Q If you turn to Page 317.

A I think one of the important parts of this paper is that they also measured that against

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the active placebo moxifloxacin. So that's critically important.

Q Okay. So you think this was a well-designed study?

A I do.

Q If you turn to Page 317. It says there: This trial demonstrated that fesoterodine does not affect the QTc interval in healthy subjects aged 45 to 65 after a therapeutic (4 milligram) or a supratherapeutic dose (28 milligrams) of fesoterodine. Do you see that?

A Yes.

Q Okay. So does that -- why would you study a supratherapeutic dose as high as 28 milligrams?

A People -- people overdose, No. 1. And just to show what the -- what the safety parameters of the drug are. So that's often done in -- in these kinds of -- of safety trials.

Q Okay. Now, the QT effect is -- is mentioned, as we have talked about earlier, in tolterodine's label, right?

A That's correct.

Q And so there is a QT benefit for

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fesoterodine over tolterodine; isn't that right?

A That is definitely true.

Q Okay. And that is a benefit that clinicians will take into account when they decide whether to dose a patient on -- that has OAB on fesoterodine versus tolterodine?

A Yes.

MS. WOOTEN: Objection, form.

THE WITNESS: I'm sorry.

MR. OELKE: I would like to mark as Carson Exhibit 21 a paper entitled, A comprehensive non-clinical evaluation of the CNS penetration potential of anti-muscarinic agents for the treatment of overactive bladder. By Callegari, et al. And that's Bates PFE01843446 to 3456 -- I'm sorry, 3457.

(Deposition Exhibit 21 marked.)

BY MR. OELKE:

Q Have you seen this paper before?

A Yes, I have.

Q And is this the paper where they determine that it's the -- whether an anti-muscarinic is a P-gp substrate or not is whether it will potentially penetrate into the --

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across the blood-brain barrier?

MS. WOOTEN: Objection, form.

A This is one of the papers. And actually, it's -- it's a little different from that in that the drugs will penetrate, but if there are substrates of P-gp, then the P-gp will wash them out.

So they go in but then they're flushed out. So that's -- that's kind of the important part of the P-gp system.

BY MR. OELKE:

Q Okay. And a study of whether or not 5-HMT, fesoterodine and tolterodine were P-gp substrates or not was around 2011 when this was published?

A It may be a little before but in that -- in that time frame.

Q Okay. So in 1998-1999 persons of ordinary skill would have had no idea whether or not any of those OAB drugs were P-gp substrates or not, right?

A Well, not to my knowledge.

MS. WOOTEN: Objection, form.

A Perhaps people in the laboratory knew

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that, but I don't think -- urologists certainly did not know that.

BY MR. OELKE:

Q And you're not aware of any publication that suggested that a P-gp substrate -- whether or not a -- a particular anti-muscarinic was a P-gp substrate had been studied at that point?

A I'm not aware of any.

Q And as it turns out, the fact that tolterodine is not a P-gp substrate and 5-HMT is a P-gp substrate is what any CNS side effects are attributable to those particular compounds, right?

MS. WOOTEN: Objection, form.

A It's certainly one of the -- one of the portions of that. I don't know that that's the only thing, but it's -- it's certainly one of the -- one of the issues.

BY MR. OELKE:

Q The accepted reason that there may be some CNS side effects associated with tolterodine is that it is not a P-gp substrate, right?

A Correct.

Q Okay. And that wasn't known earlier than 2010?

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A To my knowledge, not.

Q So the fact that tolterodine might -- the compound rather than 5-HMT might be causing CNS side effects was not known in the art in 1998 to 1999?

MS. WOOTEN: Objection, form.

A Can you restate that, I -- sorry, it was a little complex.

BY MR. OELKE:

Q I'm sorry, let me try that one more time.

In the 1998-1999 time frame, it was not known whether any CNS side effects from the dosing of tolterodine was attributable to either tolterodine or 5-HMT?

MS. WOOTEN: Objection, form.

A That differentiation had not been made at that time.

BY MR. OELKE:

Q And so as of that time a person of ordinary skill seeking to make a drug that would decrease those CNS side effects would not know whether to start with tolterodine or 5-HMT, right?

MS. WOOTEN: Objection, form.

A That's correct. But if you have the two

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different options, then why wouldn't you try one and the other and then see which one is most effective, fewest -- fewest CNS complications, et cetera.

BY MR. OELKE:

Q So if there was CNS side effects associated with tolterodine in 1998-1999 -- and there weren't many, right?

A There were not many.

Q Okay. But to the extent there were any, you would have had to study both tolterodine and 5-HMT and -- as lead compounds in order to make any conclusions about what ultimate compound would be -- would be beneficial in eliminating those CNS side effects?

A Of course.

MS. WOOTEN: Objection, form.

BY MR. OELKE:

Q Go to your initial expert report which is Exhibit 1.

A Okay.

Q If you go to Paragraph 79 which is on Page 25.

A Okay.

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Q If you go to the end of that -- that paragraph, it's -- it's talking about CYP2D6 metabolism but also CYP3A4 metabolism. Do you see that?

A At the end of -- oh, that's actually on 26. Okay, got it.

Q Sorry, yeah.

A Okay.

Q So at the top of that page 26, it starts: Additionally, there was also a concern about CYP450 metabolism of tolterodine.

It says: Tolterodine metabolism is mediated by CYP450 2D6, and in patients with poor metabolism of CYP450 2D6, dealkylation occurs via CYP450 3A4. Do you see that?

A Yes.

Q Indeed, tolterodine's label requires that in patients receiving CYP450 3A4 inhibitors, the maximum daily dose of tolterodine should be 1 milligram twice a day. Do you see that?

A Yes.

Q Okay. So we talked earlier about the studies that -- that have looked at CYP2D6 and the determination that poor metabolizers and extensive

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metabolizers received the same net effect.

But with respect to 3A4, there's no suggestion that 3A4 metabolism of tolterodine creates any risk for patients, is there?

MS. WOOTEN: Objection, form.

A If there's -- if there's more 3A4 metabolism, then the drug isn't going to act as well, isn't going to work as well.

And if -- and if there's less 3A4, which is the more common thing in the -- in clinical practice, then the drug could be around longer.

So you could overdose the patient potentially if it -- if you really -- if the entire cascade of events was -- was -- was through the -- the 3A4 pathway.

BY MR. OELKE:

Q But the 3A4 pathway is the resulting metabolite that is -- is a dealkylated version, right, of tolterodine?

A That's correct.

Q And there's no indication that that metabolite has any -- presents any toxicity risk, is there?

A No.

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MS. WOOTEN: Objection, form.

A No, there's not, but that's not the point. The point is that if you stop that metabolism, then the tolterodine stays around for a longer period of time.

BY MR. OELKE:

Q Are you aware of any studies indicating that accumulation of tolterodine presents a risk?

MS. WOOTEN: Objection, form.

A No, but if -- but if the -- if the effective dose goes over the 4-milligram range, then -- then you're -- the things we talked about are -- are risks, things like acute urinary retention and QT abnormalities.

BY MR. OELKE:

Q Okay. But again, none of that's mentioned in the label for Detrol, is it?

MS. WOOTEN: Objection, form.

A The only thing that's mentioned is -- is the caveat that if the patient's on a 3A4 inhibitor, that you should lower the dose. So one would assume that there's a reason for that.

BY MR. OELKE:

Q What's -- what are some examples of 3A4

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inhibitors?

A Macrolide antibiotics, PDE5 inhibitors, some antidepressants, some antipsychotics.

Probably the one that's -- the macrolide antibiotics are very common and they're very strong 3A4 inhibitors. And the PDE5 inhibitors are also very strong.

Q So when you dose a patient on tolterodine, do you determine whether they have any -- they're on any 3A4 drugs?

MS. WOOTEN: Objection, form.

A I usually look at their drug list and see if there's any that -- that stand out as 3A4 --

BY MR. OELKE:

Q And does it --

A -- abnormalities.

Q I'm sorry.

Does that change your -- your dosing regimen that you prescribe them?

A It may. If they're having side effects, I may basically go to a drug that doesn't have that -- doesn't have any impact in that -- in that pathway.

Q Okay. But when you're making a decision

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whether or not to -- to treat a patient with tolterodine, you don't make a no -- a go, no-go decision on that drug based on whether they're on a 3A4 inhibitor, right?

MS. WOOTEN: Objection, form.

A Not usually, no.

BY MR. OELKE:

Q Okay. If you go to Paragraph 96 which is on Page 31. You say there: Other publications, as detailed above, suggested the same solution of removing tolterodine from the dosing schema or pathway by focusing on delivery of 5-HMT. Do you see that?

A Yes.

Q What other publications are you referring to there?

A It says, See Paragraph 83 to 85. So the Sparf publication and the Sparf report is one. I guess that's the main one.

Q Well, that's just a Sparf deposition transcript, right?

A Right.

Q So that's not a publication, is it?

A It's written, I guess, so...

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Q Well, his deposition was taken a year or two ago?

A Okay, okay.

Q So -- and Dr. -- you know Dr. Sparf is not a urologist, right?

A I do, yes.

Q He's a pharmacologist, right?

A Yes.

Q Have you ever met Dr. Sparf?

A I have not.

Q Okay. So the other publications, as detailed above, I just want to understand, do you know any other publications you're referring to there or is that just a -- a typo in the -- in the paragraph?

A That's basically --

MS. WOOTEN: Objection, form.

THE WITNESS: I'm sorry.

A It's basically the -- that deposition.

BY MR. OELKE:

Q Okay. If you look at Paragraph 82. You state there: Given this knowledge, and it's referring to the -- the Nilvebrant paper -- or statement from the Nilvebrant paper.

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A Right.

Q It says: Given this knowledge, dosing clinicians were looking at the literature and questioning why 5-HMT was not being used as the active ingredient in the pharmaceutical product for treatment of OAB. Do you see that?

A Yes.

Q But you can't identify any actual literature where there were clinicians that were questioning why 5-HMT wasn't being used as an active ingredient, right?

MS. WOOTEN: Objection, form.

A No. I mean, basically it's conversations at meetings and that kind of thing. If that's a great drug, why not use that independently. But there -- there's no specific peer review publication that states that.

BY MR. OELKE:

Q And you don't recall any conversations in the 1998-1999 time frame or before that any clinicians were saying, why isn't 5-HMT being used as an active ingredient in drugs?

A I don't recall any -- any conversations like that. It could have happened, but I don't --

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I don't recall anything like that.

Q You didn't tell anyone that, right?

A Not that I know. Not that I know of.

MR. OELKE: Let's take a break.

VIDEO TECHNICIAN: Going off the record. 1:35.

(Recess taken.)

VIDEO TECHNICIAN: Back on the record. 1:41.

BY MR. OELKE:

Q If you would turn to Exhibit 1, Paragraph 98.

A Okay.

Q The very first sentence there says: As to whether fesoterodine would be considered commercially successful or not based on metrics such as sales or shares, I cannot really give an opinion on that. Do you see that?

A Yes.

Q So you're not going to be opining on the commercial success of fesoterodine, are you?

A No, because that's really measured by the company that's marketing it more than anybody else or anything else.

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Q Okay. You're not giving opinions on commercial success, right?

A No.

Q That's not an area of expertise for you?

A It is not.

MR. OELKE: Okay. Thank you, Dr. Carson. I have no further questions for you.

THE WITNESS: Okay, thanks.

MS. WOOTEN: I don't have any follow-up for you.

THE WITNESS: Okay, great.

VIDEO TECHNICIAN: Marks the end of Video 3. Off the record. The time 1:42.

(Deposition concluded at 1:42 p.m.)

(Signature reserved.)

_____

CULLEY C. CARSON, III, M.D.

Subscribed and sworn to before me this _____ day of _____, 20__.

CULLEY C. CARSON, III, M.D.

DISCLOSURE OF NO CONTRACT

I, Judith L. Leitz Moran, do hereby disclose pursuant to Article 10.B. of the Rules and Regulations of the Board of Court Reporting of the Judicial Council of Georgia that TSG Reporting was contacted by the party taking the deposition to provide court reporting services for this deposition and there is no contract that is prohibited by O.C.G.A. Sections 15-14-37(a) and (b) or Article 7.C. of the Rules and Regulations of the Board of Court Reporting for the taking of this deposition.

There is no contract to provide reporting services between TSG Reporting or any person with whom TSG Reporting has a principal and agency relationship nor any attorney at law in this action, party to this action, party having a financial interest in this action, or agent for an attorney at law in this action, party to this action, or party having a financial interest in this action. Any and all financial arrangements beyond our usual and customary rates have been disclosed and offered to all parties.

This 7th day of September, 2016.

_____

Judith L. Leitz Moran, B-2312
Georgia Certified Court Reporter

CULLEY C. CARSON, III, M.D.
CERTIFICATE OF COURT REPORTER

STATE OF GEORGIA)
COUNTY OF FULTON)

I hereby certify that the foregoing deposition was reported as stated in the caption, and the questions and answers thereto were reduced to writing by me; that the total transcript pages 1 through 157 represent a true, correct, and complete transcript of the evidence given on August 25, 2016, by the witness, CULLEY C. CARSON, III, M.D., who was first duly sworn by me.

I further certify that I am not related to any of the parties to this action by blood or marriage; and that I am in no way interested in the outcome of this matter.

I certify that I am not disqualified for a relationship of interest under O.C.G.A. Section 9-11-28(c); I am a Georgia Certified Court Reporter here as a representative of TSG Reporting; I was contacted by TSG Reporting to provide court reporting services for this deposition; I will not be taking this deposition under any contract that is prohibited by O.C.G.A. Sections 15-14-37(a) and (b) or Article 7.C. of the Rules and Regulations of the Board of Court Reporting.

This 7th day of September, 2016.

_____
Judith L. Leitz Moran, B-2312
Georgia Certified Court Reporter

CULLEY C. CARSON, III, M.D.

----------I N D E X----------

----------E X H I B I T S----------

CULLEY C. CARSON, III, M.D.

----------E X H I B I T S (CONT.)----------

CULLEY C. CARSON, III, M.D.

----------E X H I B I T S (CONT.)----------

CULLEY C. CARSON, III, M.D.

----------E X H I B I T S (CONT.)----------

CULLEY C. CARSON, III, M.D.

----------E X H I B I T S (CONT.)----------

CULLEY C. CARSON, III, M.D.

----------E X H I B I T S (CONT.)----------

CULLEY C. CARSON, III, M.D.

ERRATA SHEET FOR THE TRANSCRIPT OF:

Case Name: Pfizer v Mylan

Dep. Date: August 25, 2016

Deponent: Culley C. Carson, III, M.D.

Pg.	Ln.	Now Reads	Should Read	Reason
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Signature of Deponent

SUBSCRIBED AND SWORN BEFORE ME

THIS _____ DAY OF _____, 20___.

_____

(NOTARY PUBLIC)

MY COMMISSION EXPIRES: _____