UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME, LLC,

Petitioner,

CASE.: IPR2024-00240

-against-

THE JOHN HOPKINS UNIVERSITY,

Patent Owner.

REMOTE DEPOSITION OF

NILS LONBERG, PH.D.

NEW YORK, NEW YORK

DECEMBER 20, 2024

REPORTED BY: KIARA MILLER

FILE NO.: 562907

MERCK EX1138
Merck Sharp & Dohme LLC v. The Johns Hopkins University
IPR2024-00649

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Deposition of NILS LONBERG, PH.D., taken on behalf of PETITIONER, at REMOTE LOCATION, New York, New York, commencing at 12:08 PM, DECEMBER 20, 2024, before Kiara Miller.

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ALSO PRESENT:

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NATHAN HELPER, PAUL HASTINGS

JINNY LIM, PAUL HASTINGS

KAREN MOREIRA, IN-HOUSE COUNSEL, MERCK

N I L S L O N B E R G, after having first been duly sworn by a Notary Public of the State of New York, was examined and testified as follows:

COURT REPORTER: Please state your name and address for the record.

THE WITNESS: Nils Lonberg, 168 Bardet Road, Woodside, California 94062.

MR. RATLIFF: Good morning. My name is Preston Ratliff. I'm with the Paul Hastings law firm on behalf of the petitioner Merck. And I'm joined today by other Paul Hastings' members representing Merck.

Jessica Stauring, Jinny Lim, Nathan Helper, Rachel Wu Hankinson. In addition to that, Ms. Karen Moreira, in-house counsel for Merck is joining us, as well as Mr. Mark Stewart.

EXAMINATION BY

MR. RATLIFF:

Q Good morning, Doctor. Will you please state your full name for the record.

A Nils Lonberg.
Q Please state your residence address.
A 168 Bardett Road, in Woodside, California 94062.
Q How are you feeling today?
A Good.
Q You understand that you're testifying under oath today, right?
A Yes.
Q Is there any reason you cannot testify truthfully today?
A No.
Q Now, you're an executive at a venture capital firm, right?
A I am an executive and resident.
Q Okay. So you're an executive and resident at a venture capital firm, right?
A I'm half time there, yes.
Q You are not an oncologist, correct?
A No.
Q You've never been an oncologist, correct?

A Correct.
Q You're not a medical doctor, correct?
A Correct.
Q You have never been a medical doctor, right?
A Correct.
Q A colorectal cancer patient has never been under your medical care, right?
A Correct.
Q A cancer patient has never been under your medical care, right?
A Correct.
Q You have never prescribed pembrolizumab to a cancer patient, right?
A Correct.
Q You have never prescribed any anti-PD1 drug to a cancer patient, right?
A Correct.
Q You have never prescribed any anti-PD1 or anti-PDL1 therapy to a cancer patient, right?
A Correct.

Q You have never prescribed any pharmaceutical compound to any cancer patient, right?
A Correct.
Q Doctor, do you have any documents with you, whether in hard copy or loaded on a computer?
A I have my declaration of October 4th, 2024 and I have my declaration of March 14th, 2024, and I have a copy of the '393 Patent.
Q Okay. And are there any markings on those documents that you have with you?
A There are no markings.
Q Any pads, post-it notes, or any highlighting of any kind?
A No.
Q Now, Doctor, you read the '393 Patent that is at issue in this case, right?
A Correct.
Q You read the entire patent, right?
A Correct.

Q When you read the '393 Patent, you understood it, correct?
A Correct.
Q You were not confused by any of the '393 Patent's contents, right?
A I was not confused.
Q And when you read the '393 Patent, the statements in the patent read to you as being truthful, right?
A Correct.
Q And when you read the patent, the statements and data in the '393 Patent read to you as being accurate in terms of the science, right?
MR. RATLIFF: Objection, form.
A Could you repeat the question.
Q Sure. When you read the '393 Patent, the statements and data in that patent read to you as being accurate in terms of the science, right?
A Correct.
Q You reviewed the file history of the

'393 Patent, right?
A I don't recall if I reviewed the file history.
Q Sitting here today, you don't recall if you reviewed the file history?
A I don't recall if documents I reviewed were the file history.
Q Okay. Let me refresh your recollection.
(Whereupon, Declaration of Dr. Nils Lonberg, dated 10-4-24 was marked as Exhibit 2072 for identification as of this date.)
Q You have your declaration with you, right?
A Yes.
Q And this is the October 4, 2024 declaration that you have?
A Yes.
Q And if you can turn to Paragraph 7 of this declaration.
Let me know when you have it, sir.
A I've got it. Yes.

Q Do you see that you say in Paragraph 7 that you reviewed the '393 Patent and it's accompanying prosecution history?
A Yes.
Q Does that refresh your recollection that you reviewed the file history for the '393 Patent?
A Yes. Example 1002 must have been the document you're referring to. Which you called file --
Q And you read the entire file history, right?
A That -- I don't recall if I read everything.
Q So you're not sure if you read everything in the file history?
A I don't know. I reviewed documents that were given to me, document 1002, but I don't know if that is the entire file history.
Q Okay. Well, in the document that was given to you, 1002, did you understand everything within that document?

A Yes.
Q And you were not confused by anything that you read in that document, Exhibit 1002, right?
A Correct.
Q Now, in your analysis for this case, you used July 10, 2015 as the critical date, right?
A Correct.
Q And JHU's counsel informed you that the critical date represents the earliest possible priority date to which the claim of the '393 Patent are entitled, right?
A I was --
Q Did you hear me, Doctor?
A I was told by the Hopkins' attorneys that the July 10th date was the critical date.
Q Right. And the Hopkins' attorneys informed you that the critical date represents the earliest possible priority date to which the claims of the '393 Patent

are entitled, right?
A I believe that would be correct. I'm just trying to understand the earliest possible, given that there were earlier priority dates.
Q Now, in your declaration, you wrote that counsel has informed me and that you understand that the critical date represents the earliest possible priority date to which the challenge claims of the '393 Patent are entitled. You wrote that, right?
A Can you tell me where that is?
Q You can take a look at Paragraph 9 of your declaration, your August 4, 2024 declaration.
Let me know when you have it, sir.
A Did you say August?
Q Sorry. October 4, 2024 declaration.
A Yes, that's correct.
Q So let me try this again so that we're clear.
JHU's counsel informed you that the

critical date represents the earliest priority date to which the claims of the '393 Patent are entitled, right?

A Yes. I think it -- I think the wording in my declaration is, "The earliest possible priority date to which the challenged claims of the '393 Patent are entitled."

Q And do you understand that all of the claims in the '393 Patent have been challenged in this case?

A Where in my declaration do I say that?

Q I'm asking you. Do you understand that each and every claim has been challenged in this case?

A I'll take your word for it.

Q I'm asking you. If you don't understand, you can just say "I don't understand that."

Sitting here today, do you have an understanding whether or not each and every one of the claims of the '393 Patent have been challenged in this case --

A I don't have an understanding --
Q -- yes or no?
A I don't have an understanding that there are claims that were not challenged.
Q Okay. Now, and you understood that the July 10, 2015 date represents the earliest possible priority date to which the challenged claims of the '393 Patent are entitled, right?
A Correct.
Q Now, in your October 4, 2024 declaration, you used the phrasing, "At the time of the invention of the '393 Patent."
Do you recall using that phrasing?
A Can you point me where in my declaration?
Q Well, let me ask you first.
Do you recall at all using that phrasing, "At the time of the invention of the '393 Patent" in your declaration?
A I would like to see where in the declaration you are referring to.

Q We'll go there. But sitting here right now, do you recall using that phrasing at the time of the invention of the '393 Patent, yes or no?
A I would like to see where in the declaration I state that.
Q So let me try my question one more time.
Sitting here right now, do you have any recollection whether or not you wrote in your declaration, the phrase, "At the time of the invention of the '393 Patent"?
MR. MILLER: Objection. Asked and answered.
A There's a hundred pages in this declaration. I don't recall, sitting here right now, every -- every phrasing.
Okay. And you appreciate I'm not asking if you recall every phrasing. I'm asking you about one specific phrase.
Do you recall, sitting here right now, whether or not you used the phrasing, "At the time of the invention of the '393 Patent" in

your declaration, yes or no?

MR. MILLER: Objection. Asked and answered.

A I'd like to get this correct, which is why I'd like to see where you're pointing to.

Q Sir, I just want to -- if you don't have a recollection right now, you can just tell me.

Do you recall right now whether or not you used the phrasing, "At the time of the invention of the '393 Patent" in your October 4, 2024 declaration?

MR. MILLER: Objection. Asked and answered.

A I don't have a recollection of the entire -- all the words in the entire declaration. And so rather than agree to a particular phrasing that you described, I would like to see where in the declaration that is written.

Q Well, sir, do you appreciate I did not ask you whether or not you had an entire

recollection of all of the words that you used in your declaration? You appreciate that, right?
A Correct.
Q You appreciate that that was not my question -- okay, great.
So let's turn to your declaration, and let's look at Paragraph 53. And in particular, I'll turn your attention to Heading F.
Let me know when you're there.
A Okay. I'm there.
Q And do you see in Heading F, you write:
State of the prior art "At the time of the invention of the '393 Patent."
Do you see that?
A Are you referring to Paragraph 53?
Q I'm referring to the Heading F.
A Oh, the heading. Sorry. I apologize.
Q No worries.
A "State of the prior art at the time of the invention of the '393 Patent," is what

Heading F says.

Q Right. So you wrote in Heading F:

State of the prior art "At the time of the invention of the '393 Patent," right?

A Correct.

Q And for clarity, what date did you consider to be "At the time of the invention of the '393 Patent"?

A July 10, 2015.

Q Okay. So it's the same date as the critical date, right?

A Correct.

Q Now, you understand that JHU filed a provisional patent application on November 13, 2014, right?

A Correct.

Q And you understand that JHU filed that provisional patent application before the time of the so-called invention date, right?

MR. MILLER: Objection, form.

A That was prior to the critical date of July 10, 2015.

Q And it was also prior to what you call, "At the time of the invention of the '393 Patent," right?
A Correct.
Q Did you ever ask anyone, as part of your work in this case, why JHU filed a provisional patent application on November 13, 2014 before the time of its so-called invention?
MR. MILLER: Objection, form.
A I don't recall any specific conversation with the John Hopkins' attorneys.
Q I'm not asking if you recall any specific conversation. My question is different.
Did you ever ask anyone, as part of your work in this case, why JHU filed a provisional patent application on November 13, 2014, before the time of it's so-called invention?
MR. MILLER: Objection, form.
A I have only spoken about this case with

the John Hopkins attorneys, so it would have been a conversation with the John Hopkins attorney and I don't recall every specific conversation.

Q And you realize I'm not asking you to recall every specific conversation that you had with the JHU attorney, right?

A Correct.

Q So my question is asking about something very specific. Let me ask it again.

Did you ever ask anyone as part of your work in this case, why JHU filed a provisional patent application on November 13, 2014, before the time of it's so called invention?

MR. MILLER: Objection. Form.

A I don't recall a specific conversation.

Q Now, you read the background of invention section of the '393 Patent, right?

A Yes. The specifications, I read the entire specification.

Q You read the entire, okay.

Now, do you have any reason to believe that what's described in the specifications of the '393 Patent is not true?
A I have no reason to believe that.
Q Do you have any reason to believe that what's described in the specification of the '393 Patent is not accurate?
A No.
Q Did you have any reason to believe that what is described in the specification of the '393 Patent is not to be believed?
A No.
Q Do you have any to reason to believe that what's described in the specification of the '393 Patent does not reflect the belief of the named JHU inventors at the time that they applied for the '393 Patent?
MR. MILLER: Objection. Form.
A Could you repeat the question.
Q Sure.
Do you have any reason to believe that what is written in the specification of the

'393 Patent, does not reflect the belief of the named JHU inventor at the time that they applied for the '393 Patent?

MR. MILLER: Same objection.

A No. I don't.

Q Now, in the specification of the '393 Patent appears to you to be an accurate representation -- actually, let me ask a different question.

Do you have a copy of the '393 Patent?

(Whereupon, US Patent No. 11,591,393 B2, dated 2-28-23 was marked as Exhibit 1001 for identification as of this date.)

A Yes, I did.

Q And can I turn your attention to Column 1 of that patent, where it says it has the title background of the invention?

Let me know when you have it.

A Yes. I have it.

Q Okay. And as part of your work in this case, you read the background of the

invention section of the '393 Patent that starts on Column 1 of the patent and continues into Column 3 of the patent?
A Yes.
Q And the background of the invention section of the '393 Patent appears to you to be an accurate representation of the state of the art at the time that the patent was applied for, right?
A Yes.
Q And that section of the patent is an accurate representation of information that was publicly known before the July 10, 2015 critical date, right?
Did you hear me, Doctor?
A Yes. I'm just looking to see if there's anything in here that would have not been known prior to the critical date.
Q Sure.
A Other than the text in the second to last paragraph in the background where they say that they recruited patients, I'm not

sure if I recall whether they -- the fact that they had recruited patients was already known publicly.

Q And when you say they had "recruited patients" are you talking about JHU and the study for which JHU was the sponsor involving MSI-High Pembrolizumab?

A I'm talking about the -- do you see the text in the second to the last paragraph of the background. I'll read it to you.

It says, to test this hypothesis --

MR. MILLER: Just go slowly when your reading.

A Sorry. We initiated -- so it's in the past tense, and then it said, we also recruited patients, so there. It's written that they did something and I don't recall when that was publicly known.

Q Okay. So let me make sure you understand my question. So I'm asking -- my question relates to the July 10, 2015 critical date and you do understand that by

the July 10, 2015 critical date, there was an understanding that the study has been ongoing, right?

A I don't -- sitting here right now, I would have to parse this language to understand whether or not they are providing information that was not yet public.

Q Okay. And do you know when the trial results were released for the study that's being described in the '393 Patent.

A Are you talking about the New England Journal paper?

Q Sure.

A Yeah, I don't have a date in the top of my head, but it would be easy to find.

Q Okay. So sitting here today, you don't know whether or not the New England Journal paper that you referred to was published before July 10, 2015 or not; is that fair?

A No. It was published after.

Q Okay. Let me ask you this question, the '393 Patent described the Phase II trial

designed to evaluate immune checkpoint blockade in patients whose tumors had or did not have MMR deficiency, right?

A That is correct.

Q And the Phase II clinical trial described in the '393 Patent is the same Phase II clinical trial announced in the MSI-High study record that you talk about in your declaration, right?

A I --

MR. MILLER: Could I have the question back, please.

Q The Phase II clinical trial described in the '393 Patent is the same Phase II clinical trial announced in the MSI-High study record that you talk about in your declaration, right?

MR. MILLER: Objection. Form.

A I don't think the patent describes that clinical trial. It refers to it and it provides some information about it.

Q Well, you would agree that the MSI-High

study record is the initial announcement of the same clinical trial later described with additional details and results in the '393 Patent, right?

A My recollection is that the study record was updated over time and so the actual final clinical trial that was published in the New England Journal and some of that data is included in this patent, is a modification of the original study record.

Q Doctor, you wrote your declaration that you signed on October 4, 2024, right?

A Correct.

Q And you signed it, you understood what you wrote, right?

A Correct.

Q Let me ask my question again.

You agree that the MSI-High study record is the initial announcement of the same clinical trial later described with additional details and results in the '393 Patent, right?

A Yes, it is the initial announcement.
Q The MSI-High study record is the initial announcement of the same clinical trial later described with additional details and results in the '393 Patent, right?
MR. MILLER: Objection. Asked and answered.
A The original study record referred to a trial that evolved and became the clinical trial that it was -- that generated the data that was provided in the '393 Patent.
Q And Doctor, didn't you submit sworn testimony in your declaration stating:
"The MSI-High study record is the initial announcement of the same clinical trial later described with additional details and results in the '393 Patent"?
A Can you point to where in the declaration that quote comes from.
Q We can take a look at Paragraph 67 of your August 4, 2024 declaration, let me know

when you have it, sir?
A Yes. That's correct.
Q Let me ask my question because I want to make sure it's clear.
You agree this MSI-High study record is the initial announcement of the same clinical trial later described with additional details and results in the '393 Patent, right?
A Correct.
Q And to your knowledge all of the figures, tables, and clinical data within the '393 Patent come from that clinical trial that was initially announced in the MSI-High study record, right?
A I'm just looking at the figures, you asked if all the figures are derived from the clinical trial.
Q I'll say my question again.
To your knowledge all of the figures, tables, and clinical data within the '393 Patent comes from the clinical trial that was initially announced in the MSI-High study

record, right?
A Yeah, I'm just looking at the figures.
Q Sure.
A Looking at this right now I don't find any figures that are not derived from that clinical trial.
Q Okay. So that was an answer to part of my question, so let me just ask the rest.
To your knowledge, all of the tables and clinical data within the '393 Patent come from that clinical trial initially announced in the MSI-High study record, right?
A I'm just going to review the tables.
Q Sure.
A Yes. The tables are all derived from the clinical trials.
Q Okay. And the other part of my question is about the clinical data, so let me ask it so we're clear.
To your knowledge, the clinical data within the '393 Patent comes from the clinical trial initially announced in the

MSI-High study record, right?
A I'm just looking at the examples.
That's correct.
Q And to your knowledge, the support for the claims of the '393 Patent come from that clinical trial that was initially announced in the MSI-High study records, right?
A Correct.
Q Now, you read each of the '393 Patent claims, right?
A Yes.
Q And there are 42 claims in the '393 Patent, right?
A Correct.
Q And you understood every one of those 42 claims when you read them, right?
A Correct.
Q You were not confused by anything written in those 42 claims, right?
A I was not confused.
Q If asked you could explain the meaning of any language in those claims, right?

A Correct.
Q Now, Claim 1 of the '393 Patent is a method of treating MSI-High colorectal cancer in a human patient, right?
A Correct.
Q You understand that clinical oncologists treat cancer patients, right?
A Correct.
Q Do you believe that a clinical oncologist would need specialized experience researching and or developing new treatment for cancer for that clinical oncologist to understand the steps of the method of Claim 1?
A No.
Q You would agree the method in Claim 1 of the '393 Patent, is a cancer patient treatment method and not a method for conducting immunology research, right?
A Correct.
Q You would agree the method in the Claim 1 is a cancer treatment method and not

a method for conducting genetic research, right?
A Correct.
Q Claims 2 through 13 of the '393 Patent are methods of treating MSI-High colorectal cancer in a human patient, right?
A Correct.
Q Claims 31 through 42 are methods of treating MSI-High colorectal cancer in a human patient, right?
A Correct.
Q You would agree that the methods in Claims 2 to 13, 31 through 42 of the '393 Patent are cancer patient treatment methods and not methods for conducting immunology research, right?
A Correct.
Q You would agree that the methods in Claims 2 to 13, 31 to 42 of the '393 Patent are cancer patient treatment methods and not methods for conducting genetics research, right?

A Correct.
Q Turning your attention to Claim 14, Claim 14 of the '393 Patent, is a method of reducing the risk of cancer progression or increasing overall survival in a human patient who has MSI-High colorectal cancer patients, right?
A Correct.
Q You would agree that part of the duty of a clinical oncologist is to attempt to reduce the risk of cancer progression in cancer patients under their care, right?
A Correct.
Q You would agree that part of the duty of clinical oncologists is to attempt to increase overall survival in a human patient under their care who have cancer, right?
A Correct.
Q Do you believe that a clinical oncologist would need specialized experience researching and/or developing new treatments for cancer to understand the method of

Claim 14 of the '393 Patent?
A Could you repeat the question?
Q Sure.
Do you believe that a clinical oncologist would need specialized experience researching and/or developing new treatments for cancer to understand the method of Claim 14 of the '393 Patent?
A No.
Q You would agree that the methods in Claim 14 of the '393 Patent are cancer patient treatment methods and not methods for conducting immunology research, right?
A Correct.
Q You would agree that the methods in Claim 14 are cancer patient treatment methods and not methods for conducting genetics research, right?
A Correct.
Q Turning your attention to Claims 15 through 30 of the '393 Patent. Doctor, Claims 15 through 30 are methods of reducing

the risk of cancer progression or increasing overall survival in a human patient who has MSI-high colorectal cancer, right?

A Correct. They're all dependent on Claim 14.

Q Okay. And you would agree that the methods in Claims 15 through 30 of the '393 Patent are cancer patient treatment methods and not methods for conducting immunology research, right?

A Correct.

Q And you would agree that the methods in Claims 15 through 30 of the '393 Patent are cancer patient treatment methods and not methods for conducting genetics research, right?

A Correct.

Q Now, let me turn your attention to Claim 1 of the '393 Patent. Let me know when you have it, sir.

A I have it.

Q Do you see that the claim method of

Claim 1 contains a step of "testing, or having tested, a biological sample obtained from a patient having colorectal cancer, thereby determining that the patient's colorectal cancer is microsatellite instability high or DNA mismatch repair deficient"?

A Correct.

Q And do you see that Claim 1 of the '393 Patent also contains a step of "in response to determining that the colorectal cancer is microsatellite instability high or DNA mismatch repair deficient, treating the patient with a therapeutically effective amount of pembrolizumab"?

A Correct.

Q Other than those two steps that we've just discussed, are there any other steps of the method recited in Claim 1?

A Those are the two steps.

Q Okay. Now, would you agree that giving a MSI-High colorectal cancer patient

10 milligrams per kilogram of pembrolizumab every 14 days is an effective amount of pembrolizumab as required by Claim 1 of the '393 Patent?

MR. MILLER: Objection. Form.

A Could you repeat the dosing?

Q Let me repeat my question 'cause I want to make sure there's clarity in the record. I'll try to slow down when I get to the dosing.

Would you agree that giving a MSI-High colorectal cancer patient 10 milligrams per kilogram of pembrolizumab every 14 days is an effective amount of pembrolizumab as required by Claim 1 of the '393 Patent?

A Yeah, I just want to go back to the examples. In Example 2, "The study agent, pembrolizumab, was administered at 10 mg/kg intravenously every 14 days." So that's a correct recitation of the specification.

Q Okay. And Doctor, based on your careful read of the '393 Patent, the only dose of

pembrolizumab recited in the patent is 10 milligrams per kilogram every 14 days, right?

A I would have to go back to the specification and read it through to make sure that there's no additional references or not.

Q Okay. So sitting here today right now, you don't have an understanding whether or not beyond 10 milligrams per kilogram every 14 days there's a different dosing regimen of pembrolizumab recited in the '393 Patent; is that fair?

A I don't remember if additional dosing regimens are recited or not in the specification.

Q Okay. Now, Doctor, based on your understanding of Claim 1, does the language "effective amount of pembrolizumab," in Claim 1 include any amount of pembrolizumab beyond the 10 milligrams per kilogram every 14 days that you remember that's recited in

the '393 Patent?

MR. MILLER: Objection. Form.

A I think the language in the claim is quite clear. It says "a therapeutically effective amount." So whatever amount is therapeutically effective would be included under the claim. And there are a number of different dosing regimens for pembrolizumab, including now a hyaluronidase coformulation, that is a different but also effective amount of pembrolizumab.

Q Okay. So sitting here today, it's your understanding that when Claim 1 recites "effective amount of pembrolizumab," that can include amounts of pembrolizumab beyond the "10 milligram per kilogram every 14 days" regimen that you recall as being recited in the '393 Patent; is that fair?

A When you say "beyond," are you saying a greater amount?

Q Any additional amount.

A Any additional beyond 10 milligrams? So

added to, like 11?
Q No. Let me try my question again.
Based on your understanding of the language in Claim 1 that says "effective amount of pembrolizumab," is it your belief that an effective amount of pembrolizumab could be a dosing regimen other than the 10 milligrams per kilogram every 14 days that's recited in the '393 Patent?
A I think the language is quite clear. It's whatever is an effective amount. And it was known, and in fact incorporated by reference in the patent, that there are other amounts of pembrolizumab where activity had been seen in other cancers. So I think it's inherent within the specification that 10 milligrams per kilogram every 14 days is not a limitation.
Q Do you know whether or not the specification actually identifies any dosing regimen for pembrolizumab other than 10 milligrams per kilogram every 14 days?

A Well, the specification includes 53 references, and my memory is that some of those references include clinical trials that had explored different doses. I would have to go back and look at those references to make sure that my recollection is correct.
Q And any of those 53 references that you're talking, are any of them references where pembrolizumab was given to a MSI-High colorectal cancer patient?
A I would have to go back and go through the references.
Q And sitting here today, you just don't know, right?
A I don't recall, but I do think that other dosing regimens would be inherent and that anyone reading the claim would understand that there are different dosing regimens that are possible. For example, dosing higher and less frequently or lower and more frequently would provide for the same coverage.

Q Now, Doctor, you hold the belief that an oncologist prescribing KEYTRUDA to a colorectal cancer patient under the colorectal-related indications in the KEYTRUDA package insert would necessarily practice the method of treatment in at least Claim 1 of the '393 Patent, right?
A That's correct.
Q And it is your understanding that the recommended dosage for KEYTRUDA for the MSI-High indications in the package insert is different than the 10 milligrams per kilogram every 14 days that you recall being recited in the '393 Patent, right?
A I'm not surprised. The dosing regimen for pembrolizumab evolved over time. There was a lot of pressure to move to a less frequent dosing, and so everyone in the industry was moving their checkpoint blockade therapies toward less frequent dosing.
Q And, Doctor, I wasn't asking you if you were surprised. My question is different.

You understand that the recommended dosage of KEYTRUDA for the MSI-High indications and its package insert are different from the "10 milligram per kilogram every 14 day" dosing regimen that you recall being recited in the '393 Patent, right?

A It's to me irrelevant because all that's important is what is -- what is the PK. Do you get a similar coverage of your drug in the blood with a different dosing regimen? I think that's inherent, and anyone skilled in the art would understand that.

Q So I understand you have positions, Doctor, but I'd like an answer to my question.

And so my question is you understand that the recommended dosage for giving KEYTRUDA to MSI-High phenotypes in the package insert is different from the "10 milligrams per kilogram every 14 day" regimen that you recall being cited in the '393 Patent, right?

A Yeah, I guess I'd like to see the package insert, but again, I wouldn't be surprised.
Q Okay. So sitting here today, you don't know if it's different or not?
A I would assume it's different, given that is no longer -- the two-week dosing is no longer what is being used for pembrolizumab. I would not expect it to be the same.
Q Okay. And are you aware of any evidence demonstrating that since the conclusion of the clinical trial described in the MSI-High study records, any clinical oncologist has ever prescribed KEYTRUDA to an MSI-High patient in the amount of 10 milligrams per kilograms every 14 days?
A I -- there's no way I would know that.
Q So I just want to -- let me try my question again, just make sure I have a clear answer.
Are you aware of any evidence

demonstrating that since the conclusion of the clinical trial described in the MSI-High study records, any clinical oncologist has ever prescribed KEYTRUDA to a MSI-High patient in the amount of 10 milligrams per kilograms every 14 days?

A There is no database that covers how every patient is treated. There's no way that anyone could know the answer to that question.

Q Doctor, I'm not asking you about anyone. I'm not asking you about a database. I'm asking specifically about you.

Doctor, are you aware of any evidence demonstrating that since the conclusion of the clinical trial described in the MSI-High study records, any clinical oncologist has ever prescribed KEYTRUDA to an MSI-High patient in the amount of 10 milligrams per kilograms every 14 days? If you're not aware, you could just say that.

MR. MILLER: Objection. Form. Asked

and answered.
A Sitting here right now, I don't have a recollection.
Q And is it your belief that at some point in time you were aware of evidence demonstrating that since the conclusion of the clinical trial described in the MSI-High study record, a clinical oncologist prescribed KEYTRUDA to an MSI-High patient in the amount of 10 milligrams per kilogram every 14 days?
A I don't have a recollection.
Q So, Doctor, the JHU-named inventors on the '393 Patent were not the first persons to give a cancer patient 10 milligrams per kilogram of pembrolizumab every 14 days, right?
A That is correct.
Q And at the time of the critical date, July 10, 2015, you would agree that the person of ordinary skill in the art would know that to determine MSI-High status, tumor

tissue or bodily fluid could be tested, right?
A Correct. The standard procedure is tumor tissue. Bodily fluid requires a more specialized assay.
Q And at the time of the critical date, July 10, 2015, you would agree that testing a patient for MSI status could be accomplished by carrying out a PCR test, right?
A That was the initial standard assay for MSI-High, but at the time of the critical date, it was being overtaken by a different assay.
Q Okay. Doctor, I'm not asking about what's the initial standard. I'm asking a different question, and it's this: At the time of the critical date, July 10, 2015, you would agree that testing a patient for MSI-High status could be accomplished by carrying out a PCR test, right?
A Yes. "Could" is the critical part of that answer, yes.

Q I didn't say anything different.
So, Doctor, at the time of the critical date, July 10, 2015, you would agree that testing a patient for MSI-High status could be accomplished by carrying out a next-generation sequencing on a sample, right?
MR. MILLER: I'm sorry. Could I have the question back?
Q At the time of the critical date, July 10, 2015, you would agree that testing a patient for MSI-High status could be accomplished by carrying out a next-generation sequencing test on a sample, right?
A I would have to refresh my memory as to the availability of that particular assay.
Q Okay. Sitting here today, you don't know if that assay was available before July 10, 2015, right? Is that fair?
A That's fair.
Q Okay. Would you agree that at the time

of the critical date, testing a patient for MSI-High status could be established by carrying out an immunology history chemistry test?

MR. MILLER: Objection. Form.

A Yes. That was probably the most frequently employed assay at the critical date.

Q The JHU-named inventors on the '393 Patent were not the first persons to test a biological sample to determine if a cancer patient is MSI-High, right?

A That's correct.

Q The JHU-named inventors on the '393 Patent did not invent testing a biological sample to determine if a cancer patient is MSI-High, right?

A That's correct.

Q The JHU-named inventors were not the first persons to use a PCR test to determine if a cancer patient was MSI-High, right?

A That's correct.

Q The JHU-named inventors of the '393 Patent were not the first persons to use next-generation sequencing to determine if a cancer patient was MSI-High, right?
A That's correct.
Q The JHU inventors of the '393 Patent were not the first persons to use an immunohistochemistry test to determine if a cancer patient was MSI-High, right?
A That's correct.
Q The JHU-named inventors of the '393 Patent did not invent using PCR to carry out testing to determine MSI-High status, right?
A That is correct.
Q The JHU-named inventors of the '393 Patent did not invent using next-generation sequencing to carry out testing to determine MSI-High status, right?
A That is correct.
Q The JHU-named inventors of the '393 Patent did not invent using an

immunohistochemistry test to carry out testing to determine MSI-High status, right?
A That is correct.
Q Now, I'd like to turn your attention to Claim 14 of the '393 Patent. Let me know when you have it, sir.
MR. MILLER: Preston, this seems like a transition point. We've been going for an hour. Do you want to take a break at this point?
MR. RATLIFF: Doctor, would you like to take a break now?
THE WITNESS: Yes.
MR. RATLIFF: Okay. Let's take a break.
(Whereupon, a recess was taken from 1:09 PM until 1:27 PM.)
Q Doctor, during your break, did you discuss this case at all?
A No.
Q And during the break, did you discuss any of your testimony today?

A No.
Q Doctor, are you being paid for your work on this case?
A Yes.
Q How much are you being paid?
A I don't recall.
Q Sitting here today, you don't have a recollection how much you're being paid for your work on this case?
A It's chump change. I'm not doing this for the money. It doesn't -- the amount of money I'm making off this case is a trivial component of my income.
Q And, Doctor, you understand I didn't ask anything about your income or whether or not, how much money you are making off this case, how it related to your income.
You understand that, right?
A I'm sorry. What's the question?
Q Sure. The question is, do you understand that in my questions about how much you were being compensated, I'm not

asking how much your compensation relates to your income.

Do you understand that?

A Okay.

Q So let me try a different question.

Are you charging in this case for your work by hour or --

A Yes.

Q -- or what is the arrangement that you have?

A I'm billing per hour.

Q You're billing per hour?

A Yes.

Q And sitting here today, you have no idea how much you're billing per hour?

A I don't recall, no.

Q And how much you're billing per hour, is that reflected in some agreement that you have?

A Yes.

Q With JHU?

A Yes.

Q And what agreement is that?
A It is an agreement with Fish & Richardson.
Q Okay. And how many hours approximately have you spent working on this case?
A I don't recall.
Q Do you have a standard rate for consulting in patent cases?
A I don't have a single rate, no, but my recollection is that I am billing John Hopkins or billing Fish & Richardson less than what I have billed in the past. I again, I'm not doing this for the money.
Q And, sir, you understand, I didn't ask if you were doing this for the money. You understand that, right?
A Okay.
Q So my question is, do you know how many hours you've spent so far on this case?
A I don't recall.
Q Sitting here today, you have no idea how much time you've spent working on this case,

is that fair?
A I don't have a recollection.
Q Okay. Now, turning to Claim 14 of the '393 Patent. Let me know when you're there, sir.
A Okay.
Q Would you agree with me that Claim 14 of the '393 Patent only contains two steps to accomplish the method recited in Claim 14?
A Yes. There are two steps that are recited in that claim.
Q Right. And the first step that's recited in the claim is testing or having tested a biological sample obtained from a patient having colorectal cancer, thereby determining that the patient's colorectal cancer is Microsatellite Instability-High or mismatch repair deficient, right?
A That's correct.
Q And the second step in Claim 14 of the '393 Patent is:
"In response to determining that

the colorectal cancer is Microsatellite Instability-High or DNA mismatch repair deficient, treating the patient with a therapeutically effective amount of pembrolizumab," right?

A That's correct.

Q Now I'd like to turn your attention to Claims 31, 33 and 35 in the '393 Patent.

Let me know you have it, sir.

A Yes. I have it.

Q Do you agree that Claims 31, 33 and 35 of the '393 Patent, each refer to method results?

A Yes.

Q And would you agree that those Claims 31, 33 and 35 do not recite any additional steps from the two steps we talked about in Claim 1 of the '393 Patent?

MR. MILLER: Objection, form.

A Well, determining an objective response is a radiologic end point. And so that's an additional step.

Q Doctor, where do you see an additional step?
A In Claim 31, it says:
"Wherein the method results in an objective response rate of 40 percent or higher." And to determine an objective response requires a -- typically a CT scan or some other radiologic assay, so.
Q And so looking at Claim 31, would you agree that Claim 31 does not say "determining an objective response rate"?
A I think it's in here.
Q Okay. I'm not asking what you think.
But would you agree that Claim 31 does not say "determining an objective response rate"?
A The word "determining" is not in that claim.
Q Right. And looking at Claim 33, do you believe that there's an additional step recited in Claim 33 beyond the two steps we talked about in Claim 1 of the '393 Patent?

MR. MILLER: Objection, form.
A Well, progression is, I believe they're using resist criteria, so progression would be a 20 percent or greater increase in the size of the tumors as determined by summing the longest diameter of each of the tumors, each of the metastases. And so that would be an additional step again, a radiologic step.
Q Would you agree that Claim 33 doesn't include the word "determining" or talk about "determining" a progressive free survival?
A I think it's inherent. It's typical. It's part of the art.
Q And do you agree that Claim 33 doesn't use the word "determining"?
A The word "determining" is not in that claim.
Q Got it. Is it your -- well, actually, let's take a look at Claim 35.
Do you believe that Claim 35 includes an additional method step other than the two method steps that we discussed in Claim 1 of

the '393 Patent?
A Well, my answer would be the same as for Claim 33 and 31, in that there is a determination of progressions, that is an additional step.
Q Would you agree that Claim 35 doesn't include the word "determining" anywhere in the claim?
A Again, it's inherent.
Q I didn't ask you if it was inherent.
I'm asking you, do you see the word "determining" in Claim 35 of the '393 Patent?
A The word "determining" is not in that claim.
Q Okay. Now, is it your belief for someone to practice the methods of Claim 31, 33, and 35, that they actually have to determine the objective response rate and determine the probability of progression-free survival to practice those claims?
MR. MILLER: Objection to the form of the question.

A You would practice a claim as described in Claim 1. And then, to understand whether or not you're falling under 35, you would require that additional step of determining either response or progression.

Q So let me make sure we're clear.

To understand whether or not someone were practicing the methods of Claims 31, 33 and 35, it's your belief that you would have to have evidence that the person actually determined the objective response rate, and determined the probability of progression-free survival?

MR. MILLER: Object to the form of the question.

A The way you phrased that was a little bit inelegant, because you have to -- a determination would have to be made to know whether or not there was progression-free survival or response.

Q Okay. So let's take it claim by claim because I want to make sure I understand you.

Are you saying that for Claim 31, in order for someone to practice that claim, they actually have to do a determination of the objective response rate; is that fair?

MR. MILLER: Objection to the form of the question.

A To know whether or not the claim covered the method, you would have to determine objective response rate.

Q Are you finished with the answer?

A Yes.

Q Right. So to know whether or not if your activity is covered by Claim 31, you would actually have to determine the objective response rate; is that right?

MR. MILLER: Objection to the form of the question.

A That's correct.

Q Okay. And Claim 31 refers to colorectal cancer patients in the plural. As you understand it, who are these -- who is this group of patients in the plural?

A The patients who are being treated.
Q Is that every patient in the United States?
MR. MILLER: Objection, form.
A I don't think there's a territorial limitation.
Q So to be covered under this claim, you would have to do a determination of objective response rate based upon every colorectal cancer patient that's been treated. Is that what you're saying?
MR. MILLER: Objection to the form of the question.
A No.
Q So what's a group of colorectal cancer patients that you would have to make this objective response rate determination on --
A A --
Q -- in using Claim 31? Go ahead.
MR. MILLER: Objection to the form of the question.
A A statistically significant number of

patients.
Q And how many patients is that?
MR. MILLER: Objection to the form of the question.
A I'm not a statistician.
Q So sitting here today, you don't how many patients you would need to treat and to be covered under the method of Claim 31; is that fair?
MR. MILLER: Objection, form.
A I would have to do some work to determine that.
Q And looking at Claim 33, it also refers to colorectal cancer patients in the plural.
Do you see that?
A Yes.
Q And how many colorectal cancer patients does this claim refer to, as you understand?
MR. MILLER: Objection, form.
A A statistically significant number of patients.
Q And how many patients is that for

Claim 33 of the '393 Patent?

MR. MILLER: Objection, form.

A Again, I would have to do some work to determine that.

Q You haven't determined that as part of your work in this case so far, right?

A I don't recall. The number of patients that were analyzed in the clinical trial was enough to provide statistical significance for end points like progression-free survival or objective response rate, but I don't recall at what week that statistical significance falls off.

Q I'm asking a different question.

In your work in this case, did you determine how many colorectal cancer patients would need to be treated to be covered under the method of Claim 33?

MR. MILLER: Objection, form.

A I read the New England Journal paper, and my opinion is that the statistical analysis was correct in that paper.

Q So, Doctor, I didn't ask you if you read the New England Journal of Medicine paper. And I didn't ask you if the statistical analysis in that paper was correct. My question is very different.

I'm asking you, Doctor, as part of your work in this case, did you ever make a determination as to how many colorectal cancer patients someone would need to treat to be covered under Claim 33 of the '393 Patent?

MR.MILLER: Objection, form.

Q Did you ever do that?

A I don't recall.

Q Now, looking at Claim 35, you see that claim also refers to colorectal cancer patients in the plural, right?

A Correct.

Q Did you ever do any work in this case to determine how many colorectal cancer patients someone would need to treat to be covered by Claim 35 of the '393 Patent?

MR. MILLER: Objection, form.
A I don't recall.
Q Now, with respect to -- let me turn your attention to Claims 37, 39 and 41.
Do you agree that each of those claims refer to method results?
A Yes.
Q And do you agree that those claims do not recite any additional steps from the two steps that we talked about in Claim 29 of the '393 Patent?
MR. MILLER: Objection, form.
A The additional step would be a determination of either response rate or progression.
Q So for Claims 37, 39 and 41, it's your belief that there's an additional step of determining objective response rate or probability of progression-free survival, even though the claims do not contain the word "determining"; is that fair?
MR. MILLER: Objection, form.

A I don't think determining is required, given that it's inherent.
Q Are you saying actually making a determination of objective response rate or probability of progression-free survival as to Claims 37, 39 and 41 are inherent?
MR. MILLER: Objection. I'm sorry, could I have the question back?
Q Doctor, do you understand my question?
A I'd like to have you repeat the question.
Q That's okay. I'll rephrase it.
Doctor, is it your opinion that Claims 37, 39 and 41 have a step of requiring that the colorectal cancer patients referred to in those claims has to be statistically significant so that you can make a determination of objective response rate in the probability of progression-free survival?
MR. MILLER: Objection. Form. Scope.
A I would like you to repeat that question, because I'm a little bit unclear

because it was a rather long multi-part question.

Q Sure. Let's look at Claim 37.

With respect to Claim 37, do you believe to be covered by that claim, you would actually have to make a determination of what is the objective response rate on a group of colorectal cancer patients that were treated?

MR. MILLER: Objection. Form. Scope.

A To understand whether or not Claim 37 is relevant you would need to have an objective response rate determination made.

Q What do you mean by to understand if Claim 37 is relevant?

A Whether it covers the method of the invention.

Q So my question is to understand whether or not you're actually practicing Claim 37 and covered by that method, does the person actually have to do a determination of the objective response rate based upon a group of colorectal cancer patients?

MR. MILLER: Objection. Form and scope.

A Who's the person you're referring to?

Q Well, Doctor, in your declaration you make the claim that an oncologist prescribing KEYTRUDA to a colorectal cancer patient under the colorectal related indication described on the package insert would necessarily practice the method of treatment claimed in at least Claim 1 of the '393 Patent, right, do you remember that?

A Can you tell me where in the declaration that is?

Q Sitting here right now, you don't remember saying that in your declaration?

A I can find it pretty easily. Let me look in the index.

Q Well, I didn't ask you to go find it. I'm asking you, sitting here right now, do you remember saying that, yes or no?

A Okay. To answer the question, I'm going to right now look through the index and I'm

going to go now towards the end of my declaration and, I believe that what you're referring to is at -- is close to the end of the declaration, so I'm just trying to get there. I think I'm pretty close to it, I'm getting there.

Q Let me extend my question. Without looking at your declaration do you understand that --

A You don't want me look at my declaration?

MR. MILLER: Let him finish, go ahead.

Q That's right. Right now my question is focused on this.

Without looking at your declaration and sitting here today, do you have any recollection giving sworn testimony, that an oncologist prescribing KEYTRUDA to a colorectal cancer patient under the colorectal related indication described in the package insert would necessarily practice the method of treatment claimed in at least

Claim 1 of the '393 Patent?

MR. MILLER: Objection. Form.

Q Yes or no?

A My recollection is that is what I wrote, but to check that and make sure given that there's a lot of words in the declaration, I would like to look at the exact words, in which my memory is very close to the end of my declaration it would be very easy for me to look at that.

Q That's fine. My question is focused on something different. Now I appreciate what your state of mind right now and your current recollection.

So if you could, Doctor, turn to Paragraph 190 of your declaration, and let me know when you have it. And this is your October 4, 2024 declaration.

A Yes. That's correct.

Q So my question for you is: You say at least Claim 1 of the '393 Patent in Paragraph 190 of your declaration, other than

Claim 1, are there any additional claims that you believe would be necessarily practiced by the method of treatment -- sorry, let me start over.

Other than Claim 1 of the '393 Patent, do you believe that there would be any other methods necessarily practiced if an oncologist is prescribing KEYTRUDA to a CRC patient under the CRC related indications in the package insert?

MR. MILLER: Objection. Form.

A I would have to go back and do some work to identify which are the relevant claims.

Q I'm not sure if I asked -- I'm not asking about the relevant claims.

In your declaration you say that if an oncologist is following the package insert, they would necessarily practice the method of treatment claimed in at least Claim 1 of '393 Patent.

So my question is: Beyond Claim 1, are there any additional claims in the '393

Patent for which you hold that same belief?
MR. MILLER: Objection. Form. Asked and answered.
A I don't understand why the word "relevant" is unclear.
Q Did you hear my question?
A Yeah, I'm asking you why isn't relevant the right -- what is unclear about the word relevant.
Q Let me try my question 'cause I don't understand what you're asking me. So let me try my question again.
Sitting here today, do you believe that if an oncologist prescribes KEYTRUDA to a CRC patient under the CRC related conditions in the practiced insert, they would necessarily practice the method of treatment claimed in any claim of the '393 Patent other than Claim 1?
MR. MILLER: Objection. Form.
A I thought that I answered that. I said I would have to do some work to identify

which claims are relevant.
Q Okay. And you haven't done that work so far in this case, right?
A I think my recollection is I have. But I don't recall the determination that I made.
Q So you believe that you had made a determination looking at the 42 claims in the '393 Patent whether or not an oncologist would necessarily be practicing the method of the '393 Patent?
A That is my recollection.
Q Okay. Let's take a look at one. Looking at Claim 31 of the '393 Patent.
Let me know when you have that?
A Yes, I do.
Q And do you believe if an oncologist followed the method -- strike that.
Do you believe if an oncologist followed the prescribing, the recommended prescribing method for CRC patient under the CRC related indications in the package insert that the oncologist would necessarily be practicing

treatment method of Claim 31?
MR. MILLER: Objection. Form and scope.
A I would have to do a little bit of work.
Q Sitting here today, do you know, do you have an opinion?
A I'd have to do a little bit of work.
Q Sitting here today, do you have an opinion, if you know?
A Again, I would have to do a little bit of work to do that, to determine that.
Q I just want to make sure I'm clear. Sitting here today, do you know with respect to Claim 31?
A I don't recall.
Q Do you know with respect to Claim 33?
A Again, I would have to do some work. I don't recall my determination on the individual claims.
Q And did you make a determination with respect to Claim 35?
A Yes.

Q And is it your opinion, that if an oncologist prescribes KEYTRUDA according to the CRC-related indication in the package insert, the oncologist would necessarily be practicing the method of Claim 35 of this '393 Patent?

MR. MILLER: Objection. Form and scope.

A I don't recall my determination.

Q Do you recall your determination for that same question as to Claim 7 of the '393 Patent?

MR. MILLER: Objection. Form and scope.

A I don't recall.

Q And do you recall if you made a determination with respect to that same question as to Claim 39 of the '393 Patent?

MR. MILLER: Objection. Form and scope.

A I don't recall.

Q Do you recall with respect to that same

question, if you made a determination with respect to Claim 31 of the '393 Patent?

MR. MILLER: Objection. Form and scope.

A I recall I made a determination I may have answered the previous question too quickly because I also recall that I made a determination. I just don't recall the results of that determination.

Q And if you made that determination, would it be in your declaration?

A Not necessarily.

Q Okay. So it could be something that you're just not testifying to, right?

A Not all the determinations that I made are in the declaration, no.

Q All right. I want to just be sure we're really clear about this. Turning your attention to Paragraph 190 of your declaration and your statement where you say an oncologist prescribes KEYTRUDA to CRC patient under the CRC-related indications

described above would necessarily practice the method of treatment claimed in at least Claim 1 of the '393 Patent, sitting here today, can you name any claim, other than Claim 1, that you're talking about in that space?

MR. MILLER: Objection. Form and scope.

A I don't recall, no.

Q Now, the determination steps that you believe is in Claim 31, 33, 35, 37, 39, and 41 of the '393 Patent, were those steps to make that determination in your view known publicly as of the July 10, 2015 critical date?

A Yes. And they're also clearly disclosed in the specification.

Q Now, looking again at Claims 31, 33, 35, 37, 39, and 41 of the '393 Patent, you understand that each of those claims refer to colorectal cancer patients in the plural, right?

A Correct.
Q And would you agree that an objective response rate would not apply to a single patient that's treated?
MR. MILLER: Objection. Form.
A It would apply, it just wouldn't be determinable from a single patient.
Q Okay. So you would agree that you could not determine an objective response rate if you only treated a single patient; is that fair?
MR. MILLER: Objection. Form.
A That's correct.
Q And is it also fair that the probability of progression-free survival at 20 weeks would also not be determinable if you were only treating a single patient?
MR. MILLER: Objection. Form.
A That's correct.
Q And would you agree with respect to these claims that the probability of progression-free survival could also not be

determined if you were only treating a single colorectal cancer patient?

MR. MILLER: Objection. Form.

A That's correct.

Q Now, as part of your work on this case you reviewed the MSI-High study record, right?

A Yes.

Q And you understand that before the critical date the study record was posted publicly in clinicaltrials.gov, right?

A Correct.

Q You reviewed the study record carefully, right?

A Correct.

Q And you reviewed the study record objectively, right?

A Correct.

Q You reviewed the study record without any bias whatsoever, right?

A Correct.

Q And JHU's counsel informed you that you

should consider the study record through the lens of one of ordinary skill in the art at the time of the July 10, 2015 critical date, right?

A Correct.

Q And did you consider the study record with that lens?

A Yes.

Q And do you believe that you understand how a person of ordinary skill would have read and understood the study record?

A Correct.

Q And you would agree that the person of ordinary skill would not read the study record with any bias, right?

A Correct.

Q And you would agree that the person of ordinary skill would not read the study record in an illogical way, right?

A Correct.

Q And you understand that all prior art references such as the posted study records,

are to be looked at from the viewpoint of the person of ordinary skill in the art, right?
A Correct.
Q And would you agree that if the person of ordinary skill set out to conduct the clinical trial disclosed in the study record, the person of ordinary skill would perceive rationally, right?
MR. MILLER: Objection. Form.
A Correct.
Q You would agree that if the person of ordinary skill set out to conduct a clinical trial disclosed in the study record, a person of ordinary skill would proceed logically, right?
MR. MILLER: Objection. Form.
A Correct.
Q And you understand that the person of ordinary skill has ordinary creativity, right?
MR. MILLER: Objection. Form.
A Correct.

Q And you understand that the person of ordinary skill can make inferences and creative steps, right?
A Correct.
Q And you understand that the person of ordinary skill has ordinary creativity and is not an automaton, right?
A Correct.
Q And you would agree that the person of ordinary skill does not doubt the literature that that person reads, right?
MR. MILLER: Objection. Form.
Go ahead.
A I think a person of ordinary skill in the art reads the literature skeptically, always.
Q Right. So it's your belief that the person of ordinary skill, when that person reads the literature, they're reading it skeptically; is that fair?
A The person of ordinary skill in the art would be a scientist, and scientists always

question everything they read.
Q Okay. And so in your view, the person of ordinary skill would be questioning every prior art reference that they read and have knowledge of, right?
A They would have a questioning attitude toward it. They would read it carefully and try to understand whether they -- whether the assertions in the particular publication were justified.
Q Okay. And is it your belief that the person of ordinary skill would distrust statements that are published in the scientific literature?
MR. MILLER: Objection. Form.
A I don't think -- "distrust" implies something that I'm not trying to describe. What I'm trying to describe is the scientific method, if you will, where every hypothesis has to be tested. And so that is a skeptical lens.
And so yes, it is distrustful by nature,

but I'm also aware of the way "distrustful" shows up in the English language. And so I'm a little concerned that you might not be capturing the skeptical lens that is part of the scientific method.

Q Right. And for your work in this case, when you view the prior art from the perspective of the person of ordinary skill in the art, you applied a skeptical lens; is that right?

A Well, when I read the prior art, I read it trying to consider what a person of ordinary skill in the art would -- how a person of ordinary skill in the art would read that particular reference, that particular piece of prior art, whether or not they would take it at face value or not.

Q Right. And from your perspective, a person of ordinary skill in the art would naturally have a skeptical lens when looking at a piece of prior art; is that fair?

A A person of ordinary skill in the art

would have a skeptical lens when viewing any -- any scientific publication.

Q Okay. And would you agree that the person of ordinary skill in the art would have seen a trial disclosed in the study record that you discussed in your declaration, right?

A A person of ordinary skill in the art would have viewed that as a disclosure that a trial will take place. The person of ordinary skill in the art would understand that that is a regulatory requirement to post that study record.

Q But you understand that the person of -- well, let me ask you.

Would you agree that the person of ordinary skill in the art would have seen a trial disclosed in the study record?

MR. MILLER: Objection. Asked and answered.

A Again, I thought I answered that. It's a disclosure of a trial that will take place,

that is planned to take place.
Q Well, you believe that there was a trial disclosed in the MSI-High study record, right?
A Yes.
Q And so would you agree that the --
A It was a disclosure of a trial that would take place.
Q Let me try this again.
You agree that there was a trial disclosed in the MSI-High study record, right?
MR. MILLER: Objection. Asked and answered.
A Again, I thought I answered that. That trial was a planned trial, yes.
Q So you agree that there was a trial disclosed in the MSI-High study record, right?
MR. MILLER: Objection. Asked and answered.
A Yeah, the trial was planned, so I agree

with you.
Q And you agree that the POSA would have seen a trial disclosed in the study record, right?
A They would have seen that a trial was planned, yes, from the study record, so I agree.
Q And the POSA would understand that the trial is a Phase II study of the chemical compound MK-3475 in patients with microsatellite unstable tumors, right?
MR. MILLER: Objection. Form.
A My recollection is, yes, that's correct.
Q And MK-3475 is pembrolizumab, right?
A That's correct.
Q And the POSA would have seen in that study record that one of the steps for conducting the study is giving 10 milligrams per kilogram of pembrolizumab every 14 days to microsatellite instability-high colorectal cancer patients, right?
A I don't have the study record in front

of me. That sounds reasonable. But if you'd like me to confirm that, perhaps we could pull up the study record.

Q Sure. Let's bring up the study record. It's Exhibit 1005.

(Whereupon, Study NCT01876511, dated 6-10-13 was marked as Exhibit 1005 for identification as of this date.)

Q I think we can get help putting it in the chat, and then you can download it, sir.

TECH WELCH: This is the remote tech. Exhibit 1005, it's uploading to the shared folder now.

Q Just let me know when you have it, sir.

TECH WELCH: And please be mindful that you may need to refresh the page.

A Okay. I have it.

Q Okay. Now, the POSA would have seen that one of the steps for conducting the study is giving 10 milligrams per kilogram of pembrolizumab every 14 days to MSI-High

colorectal cancer patients, right?
A That is a component of the trial. That is one of the cohorts.
Q Okay. And at the time of the invention of the '393 Patent -- and this is the July 10, 2015 date -- as you understand it, it was known that a small percentage of cancer patients were MSI-High, right?
A My recollection --
MR. MILLER: Sorry.
Objection. Form.
Go ahead.
A My recollection is that at the time of the invention at July 10th, 2015, that the published numbers for the percentage of colorectal cancer patients that were MSI-High was in the range of 15 percent.
Q And so would you agree that at the time of the invention of the '393 Patent, it was known that a small percentage of cancer patients were MSI-High?
MR. MILLER: Objection. Form.

A My recollection is that the numbers were around 15 percent.
Q And so I'm asking you would you agree that at the time of the invention of the '393 Patent, it was known that a small percentage of cancer patients were MSI-High.
MR. MILLER: Objection. Asked and answered.
A I don't know why you keep using the word "small." I don't know what that means to you.
Q Sir, you have your declaration in front of you, right?
A Yes.
Q Can you turn to Paragraph 50 of your declaration. And I want to turn your attention to where you use the phrasing "small percentage of cancer patients." Just let me know when you have it.
A Okay. I have it.
Q And you see that you give sworn testimony in your declaration stating:

"At the time of the invention of the '393 Patent, it was known that a small percentage of cancer patients, including CRC patients, were MSI-High"?

A That's correct.

Q And you understood that statement when you wrote it, right?

A Correct. I understood that to be on the order of 15 percent.

Q Now, it in fact was publicly known by at least 2010 that a small percentage of cancer patients, including colorectal cancer patients, were MSI-High, right?

A That's correct.

Q And it was also known by 2010 that the tumors of MSI-High cancer patients tended to have high mutational loads and were infiltrated by immune cells, right?

A That is correct.

Q And that was publicly known by at least 2010, right?

A I don't recall the date at which the

immune cell infiltration paper came out, but the mutational load was clearly known by 2010.

Q Do you recall the publications that you cited in your declaration?

A Yes. There is a publication which was from, I think, Walter Bodmer in Nature that discussed the mutational load. But I don't recall the date of the first paper to disclose the lymphocytic infiltration. I just don't recall, sitting here right now.

Q Okay. And you realize I didn't ask you if you recall the first paper to discuss that. You realize that, right?

A Right. But I just don't -- I don't recall whether or not there was a publication prior to 2010 discussing the lymphocytic infiltration.

Q Right. And my question was not about prior to 2010. My question was that it was known at least by 2010 that the tumors of MSI-High cancer patients tended to have

higher mutational loads and were infiltrated by immune cells.

You would agree with that?

A My recollection is clearly that the mutational load was understood, and I don't understand why you are distinguishing prior to 2010 from the wording of your question.

Q Okay. Would you agree that prior to the posting of the MSI-High study record it was known that tumors of MSI-High cancer patients tended to have higher mutational loads and were infiltrated by immune cells?

A That is correct.

Q Now, the POSA, looking at the posted study record, would understand that the trial disclosed in the study record has an anticipated enrollment of 71 patients, right?

A I don't have the study records in front of me anymore locally.

Q You can bring it up. It's in Exhibit 1005.

Your counsel is helping you bring it up.

MR. RATLIFF: Thank you, Counsel.
A Okay. Could you repeat the question?
Q Sure.
You would agree that the person of ordinary skill in the art would understand that the trial disclosed in the study record has an anticipated enrollment of 71 patients, right?
A I'm just looking for that number.
Q Did you look at the study record carefully for this case?
A Yes, I did. I'm just looking for the number "71."
Q Maybe you can turn your attention to Page 4 of 6 in Exhibit 1005.
A I see it. "Enrollment: 71, Anticipated." Yes. That's correct.
Q Right. So you would agree that the person of ordinary skill in the art would understand that the trial disclosed in the study record has an anticipated enrollment of 71 patients, right?

A That's correct.
Q And you would agree that the person of ordinary skill in the art would appreciate that the study record identifies eligibility criteria, right?
A Yes.
Q And would you agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record would see for the inclusion criteria there's ten different things that are listed, right?
A Yes.
Q Now, I want to talk about those ten different points of inclusion criteria, and starting with the tenth one.
So the POSA attempting to conduct a trial disclosed in the study record would understand as part of the inclusion criteria the patient would have to agree to have a biopsy of their cancer, right?
A That's correct.
Q And you would agree that the POSA

attempting to conduct the trial disclosed in the study record would confirm that the patient actually has agreed to have a biopsy of their cancer taken before giving any patient pembrolizumab, right?

A No. That's not stated in the study record.

Q Okay. So let me just make sure I'm clear on your testimony.

You -- I'll ask this way: Would you agree that the person of ordinary skill in the art attempting to conduct the trial disclosed in the study record would confirm that the patient has actually agreed to have a biopsy of their cancer taken --

A Yes.

Q -- before giving that patient any pembrolizumab?

A They would have agreed to have a biopsy of their cancer before being entered into the trial, yes.

Q Okay. And would you agree that the

person of ordinary skill in the art attempting to conduct the trial disclosed in the study record would have to confirm that the patient was willing and able to comply with study record procedures before giving that patient any pembrolizumab, right?

A That's correct.

Q And would you agree that the POSA attempting to conduct the trial disclosed in the study record would confirm that the patient has actually signed the informed consent form before giving that patient any pembrolizumab, right?

A That's correct.

Q And that was including Criteria No. 8, and we'll go to 7, now.

Doctor, you would agree that the person of ordinary skill in the art, attempting to conduct a trial disclosed in the study record, would actually confirm that the patient has used an acceptable form of birth control through the study and for 28 days

after final dose of the study drug, before giving that patient any pembrolizumab, right?
A That's correct.
Q And, Doctor, you would agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record, would actually confirm that the patient had adequate organ function as defined by study specified laboratory tests before actually giving any patient pembrolizumab, right?
A That's correct.
Q And you would agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record, would actually confirm that the patient had a ECOG performance status of zero to one before giving any patient pembrolizumab, right?
A That's correct.
Q And that was inclusion Criteria No. 5. We'll move on to four.

You would agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record would actually confirm that the patient has measurable disease before actually giving any patient pembrolizumab, right?

A That's correct.

Q Now, looking at inclusion Criteria No. 3, would you agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record would actually confirm that noncolorectal cancer patients are actually MSI positive before giving any noncolorectal cancer patient pembrolizumab, right?

A Within the trial, yes, agreed.

Q Let me try -- I'm not sure of your response.

You would agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record, would confirm for any noncolorectal

cancer patients, that that patient actually was MSI-High positive before giving any noncolorectal cancer patients any pembrolizumab, right?

A Within the trial, yes, you're right.

Q And you would agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record, would confirm that for any colorectal cancer patient, that the colorectal cancer patient is either MSI-High positive or MSI-High negative before giving any pembrolizumab to the patient, right?

A I don't think that that requires any determination because any patient is either positive or negative. There's no third alternative.

Q So let me try my question again.

Would you agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record, would actually confirm for any

colorectal cancer patient, whether they're MSI-High positive or MSI-High negative, before giving any colorectal cancer patient pembrolizumab?

A You use the word "confirm," there's no need to confirm because there's only two possibilities, they're either positive or negative. So that determination just requires which arm to go into, arm one or arm two.

Q Let me try this question.

Would you agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record, would actually test any colorectal cancer patient to determine -- or, sorry, let me start this again.

Would you agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record, would, for the colorectal cancer patients enrolled in the study, test them to

determine whether or not they're MSI-High positive or MSI-High negative before giving them any pembrolizumab?

A No.

Q Okay. And so, in your view, of the ten inclusion criteria that's listed in the posted study record, the person of ordinary skill in the art attempting to conduct the trial disclosed in the study record would make a confirmation as to inclusion criteria three through ten before giving any patient pembrolizumab, but would not do the same for inclusion criteria one and two; is that fair?

A This is a -- this is a biomarker trial that requires a retrospective analysis. And the retrospective analysis is the impact of MSI-High positivity or negativity to the outcome of -- to the therapeutic outcome.

Q Let me try my question again because I'm not sure you understood it.

You recognize that the person of ordinary skill in the art attempting to

conduct the trial disclosed in the study record would see ten inclusion criteria, right?

A That's correct.

Q And you believe that the person of ordinary skill in the art attempting to conduct the trial disclosed in the study record would actually make a confirmation as to inclusion criteria numbered three, four, five, six, seven, eight, nine and ten, before giving any patient pembrolizumab, but would not do a confirmation as to inclusion criteria one and two?

A A person of ordinary skill in the art would be someone who is familiar with designing clinical trials. And this person is going to look at this design. They're going to say, okay, this is a biomarker trial. And there's a couple of reasons to have a sort of a biomarker trial.

One is, if you've got a diagnostic that you think is going to be a good diagnostic

for selecting patients, but that diagnostic is not yet approved, and so in order to select patients to put them into a particular arm, you would need to get what is called an investigational device exemption from the FDA. And that's a costly process.

So, typically, people who have what they think is a good assay, but it's not yet approved, they would design a trial like this. But in this case, the MSI-High diagnostic is out there and is in use, and so if you look at a trial like this, then you're thinking, well, this a trial that's designed to test multiple hypotheses.

And, particularly, you look down and see agree to have a biopsy of a cancer. I'm presuming, and I would presume as a person of ordinary skill in the art, that would include something like a PBL1 positivity for the cancer and for the tumor cells. So you're going to be looking at a lot of different biomarkers and determining which single

biomarker or set of biomarkers allows you to subset the MSI-High positive colorectal cancer patients from the MSI-High negative colorectal cancer patients in terms of outcome.

If, in fact, you were confident that you had a good diagnostic for selecting patient, you would not need arm two at all. Arm two is irrelevant. Arm two is certainly not relevant to regulatory approval and there's no MSI-High negative colorectal cancer subset in the -- in the pivotal trial for this. The -- or required for the pivotal trial for this.

And there's also, you know, given that it was known in the art that MSI-High negative colorectal cancer patients, the response rate was exceptionally low, you would be able to recognize a signal without that arm two.

But arm two, the inclusion of arm two makes a person of ordinary skill in the art

think, well, we don't really know whether or not the MSI-High positivity is going to make a substantial contribution to the patient outcome. And so we're going to look at, potentially a lot of different biomarkers.

Q And, Doctor, you would agree that the person of ordinary skill in the art attempting to conduct a trial disclosed in the study record, would know before giving any patient pembrolizumab, that a small percentage of cancer patients were MSI-High?

A At the time it would have been assumed to be on the order of 15 percent. And that's going to depend on what pool of patients you're selecting from.

Q And you equate 15 percent with being small; is that fair? 15 percent is a small percentage, in your opinion?

A It is less than half. But, again, it would depend on what the pool of patients is. I don't know what the pool of patients is.

Q Doctor, you remember in your

declaration, you say, "At the time of the invention of the '393 Patent it was known that a small percentage of cancer patients were MSI-High," you remember that, right?

A Yes. And I was referring to the 15 percent number. Which I think -- I don't remember if 15 percent is in my declaration, but certainly in references within -- that were referred to in the declaration.

Q So let me ask the question.

Would you agree that the person of ordinary skill in the art attempting to conduct the trial disclosed in the study record, before they give any patient pembrolizumab would understand that only a small percentage of cancer patients, including colorectal cancer patients, were MSI-High?

MR. MILLER: Objection, form.

Go ahead.

A I don't know what pool of patients they're selecting from.

MR. MILLER: Preston, we've been going for well over an hour. Is this a good time?

MR. RATLIFF: Dr. Lonberg, would you like to take a break?

THE WITNESS: Yes, please. Thank you.

(Whereupon, a recess was taken from 2:39 PM until 2:51 PM.)

Q Doctor, during the break, did you discuss any of your testimony?

A No.

Q During the break, did you discuss this case?

A No.

Q Doctor, do you believe that the trial disclosed in the MSI-High study record was a retrospective clinical study?

A Yes.

Q And you have read the package insert for KEYTRUDA, correct?

A Yes.

Q And do you know whether or not the

package insert for KEYTRUDA, if it describes the clinical trial disclosed in the MSI-High study record as a retrospective versus a prospective clinical study?

A I don't -- I don't recall.

Q You don't recall either way?

A No.

Q But when you read the package insert that you actually cite in your declaration, you read that carefully, right?

A Yes.

Q You weren't confused by anything in the package insert when you read it, right?

A No.

Q And you don't distrust anything that was written in the package insert, do you?

A No.

Q Do you believe that the person of ordinary skill in the art -- strike that.

Doctor, I want to turn your attention back to the '393 Patent. And in particular, we had a discussion earlier regarding

Claims 31, 33, 35, 37, 39 and 41.

So my question to you, Doctor, is, as you understand it, each of those Claims 31, 33, 35, 37, 39, and 41 of the '393 Patent, they require a statistical determination step; is that fair?

MR. MILLER: Objection, form.

A They require a determination step and the validity -- well, whether or not the claims are relevant requires a determination step, and the significance of that determination step requires a statistical analysis.

Q Is a determination step that you're referring to, is that a mathematical calculation?

A No. The determination step is -- well, it includes simple math, but it is the radiologic assay for looking at shrinkage or growth of the tumors.

Q Okay. Do the claims that we're referring to, do they have any different

clinical treatment steps other than the clinical treatment steps that we talked about in Claim 1 and Claim 14 of the '393 Patent?
A No.
Q So those Claims 31, 33, 35, 37, 38 and 41, in terms of a clinical treatment step, just have the same two clinical treatment steps that we discussed in Claims 1 and 14 of the '393 Patent, right?
A Correct. That's two steps, yes.
Q Now, the posted study record, and this is Exhibit 1005, it does not identify the trial disclosed in it as an all comers trial, right?
A The words "all comers" don't show up in the study record.
Q Right. And the person of ordinary skill, looking at the posted study record, would see that it has only three experimental arms, right?
A That is true.
Q And the person of ordinary skill would

understand that the posted study record provides that there will be both colorectal cancer patients, as well as noncolorectal cancer patients in the study, right?

A That is correct.

Q And the person of ordinary skill in the art would understand that the trial disclosed in the posted study record does not permit enrollment of patients that are MSI-High negative and had noncolorectal cancer, right?

A They would not be included in the trial.

Q Okay. And I want to be sure I got an answer to my question about the person of ordinary skill in the art.

Would you agree that the person of ordinary skill in the art would understand that the trial disclosed in the posted study record provides that there will be both colorectal cancer patients as well as noncolorectal cancer patients?

MR. MILLER: Objection, form.

A That's correct.

Q Okay. And you would agree that the person of ordinary skill in the art would understand that the trial disclosed in the posted study record does not permit enrollment of patients that are MSI-High negative and have noncolorectal cancer, right?
A That's correct.
Q And based on an objective read of the posted study records, you would agree that the person of ordinary skill in the art would understand that all noncolorectal cancer patients would need to be tested and determined their MSI-High status before giving them Pembrolizumab, right?
A Within the trial, correct.
Q And you would agree that the person of ordinary skill in the art would understand that the trial does not involve noncolorectal MSI stable patients, right?
A That's correct.
Q You would agree the person of ordinary

skill in the art would understand that the posted study record has a parallel assignment interventional study record, right?
A Can you say that again?
Q You would agree that the person of ordinary skill in the art would understand that the posted study record has a parallel assignment interventional study model, right?
A Yes. It's multiple arms with the same intervention.
Q By parallel that means the treatment for each of the three arms are given about the same time, right?
MR. MILLER: Objection. Form.
A I don't know what the -- how the actual enrollment unfolded, so I can't say that.
Q I'm asking about the meaning of parallel assignments.
You see parallel assignment in the study record, right?
A Yeah, it means it can happen, but I don't know what actually happened. I don't

know whether they filled up --
Q Okay. And I'm not asking about what actually happened. I'm asking you about your understanding of the term parallel assignment when it comes to an interventional study model.
So here's my question: A parallel assignment means that the treatment for each of the arms in the study are given about the same time, right?
MR. MILLER: Objection. Form.
A It means that they can be, but it depends, the actual timing of treatment depends on whether or not, on which arm gets enrolled first and which arm fills up first. So it's -- it doesn't -- parallel assignment doesn't imply parallel therapy.
Q Okay. So parallel assignment confers to you what then?
A It means that you are not first filling up arm one and then recruiting patients for arm two and then recruiting patients for arm

three. There's no -- that you are assigning patients for all three arms as patients come in.

Q Okay. And is it your belief that the POSA attempting to conduct the clinical trial disclosed in the study record, knowing that they would need to test noncolorectal cancer patients to determine their MSI-High status, would not at the same time attempt to test the colorectal cancer patients that are in arms one and two of the study?

A I don't think there's a requirement to report to conduct the study given that you've got two different arms, negative and positive.

Q I didn't ask if there was a requirement.

A I don't even think there's a practical requirement for it.

Q You understand that I didn't ask if there was a practical requirement, right?

A Now, you're asking that, no.

Q Would you agree that the POSA attempting

to conduct the clinical trial that's disclosed in the study record, knowing that they would need to test noncolorectal cancer patients to determine their MSI-High status, would also attempt about the same time to test the colorectal cancer patients in arms one and two to determine their MSI-High status, right?

MR. MILLER: Objection. Form.

A No.

Q Okay. Now, you read the board's institution decision, right?

A I don't recall.

Q You don't recall reading the board's institution decision?

A I don't recall.

Q Do you know what I mean by the board's institution decision?

A Yes.

Q Let's take a look at your declaration and if you could turn to Paragraph 96 and let me know if you have it, should be Page 53 of

your October 4, 2024 declaration.
A Yes.
Q So you see in Paragraph 96, you reference the board and the board's institution decision?
A Yes.
Q Sitting here today, is it correct that you read the institution decision?
A Yes.
Q And did you read it carefully?
A Yes.
Q And when you read it, did you understand it?
A Yes.
Q Now, in your opinions, the plain and ordinary meaning of the claim language in response to as used in the claims of '393 Patent requires a causal relationship, right?
A Yes.
Q And that causal relationship is between determining that a patient's colorectal cancer is Microsatellite Instability-High or

DNA mismatch repair deficient and treating the patient with pembrolizumab, right?
A Depending on the outcome.
Q Let me try that again.
In your opinion, the plain and ordinary meaning of the term in response to requires a causal relationship between one, determining that a patient's colorectal cancer is Microsatellite Instability-High or DNA mismatch repair deficient; and two, treating the patient with pembrolizumab, right?
A Right, but it's in response to the outcome of that test.
Q Now, Dr. Lonberg, do you recall giving sworn testimony in your declaration to the effect that in your opinions the plain and ordinary meaning of the term "in response to" requires a causal connection -- a causal relationship, sorry, between one, determining that a patient's colorectal cancer is Microsatellite Instability-High or DNA mismatch repair deficient; and two, treating

the patient with pembrolizumab, right?
A And that's what I was referring to because determining that it is MSI-High is dependent on the outcome of that test.
Q Now, in reading the board's institution decision, you understand that the board believes that the petitioner Merck has sufficiently shown that there is a likelihood, reasonable likelihood, of a causal relationship in the MSI-High study record between treatment of colorectal cancer patients and determination of their MSI-High status, right?
MR. MILLER: Objection. To form.
A I'd have to look at the -- I'd have to refresh my memory with the board's -- the test from the board's decision.
Q Okay. Sitting here today, right now, you don't remember what the board said?
A No.
Q Okay. Let's take a look at the institution decision paper No. 10, it's dated

June 13, 2024, and we should be able to put that in the chat so you can take a look at it.

(Whereupon, Decision Granting Institution of Inter Partes Review, dated 6-13-24 was marked as Exhibit Paper 10 for identification as of this date.)

TECH WELCH: I apologize counsel, which exhibit is that?

MR. RATLIFF: It's called paper No. 10 it's not an actual exhibit.

TECH WELCH: Understood.

MR. RATLIFF: Let me know if you're not able to find it.

TECH WELCH: I see it. Should be uploading one moment.

MR. RATLIFF: Thank you so much.

Q Dr. Lonberg, let me know when you have the board's institution decision that you said you read very carefully and that you understood.

A Okay, I have it.
Q Now, if I could turn your attention to Page 16 of the institution decision.
Are you there?
A Yes. I'm on Page 16.
Q Okay. And if I could turn your attention to it's near the top of the page of 16 where there's a sentence that begins "petitioner has sufficiently shown."
Do you see that?
A Yes.
Q And do you see that it reads, "Petitioner has sufficiently shown that there is a reasonable likelihood of a causal relationship in the MSI-High study record between treatment of colorectal cancer patients and the determination of their MSI-High status."
Do you see that?
A Yes.
Q And that was a statement that the board made, right?

A Yes.
Q So you understand that the board did not ignore the claim language in response to -- strike that.
You understand that the board did not ignore that the claim language in response to found in the claims of the '393 Patent involved a causal relationship between treatment of colorectal cancer patients and determination of their MSI-High status, right?
MR. MILLER: Objection. Form.
A That seems to be the implication because they do bring up causal relationship.
Q Now, you prepared two declarations for this matter, right?
A That's correct.
Q And there was a March 14, 2024, declaration that you prepared, right?
A That's correct.
Q We have been discussing today an October 4, 2024, declaration that you prepared,

right?
A Correct.
Q Just to be clear, you read those declarations carefully before you signed them, right?
A Excuse me, could you repeat the question.
Q Sure. Just to be clear, you read those declarations, your March 14, 2024, and your October 4, 2024, declarations carefully before you signed them, right?
A That's correct.
Q And did you understand every statement you made in those declarations before you signed them?
A Yes, I did.
Q And sitting here today, do you believe that there are any errors in your declaration?
A No.
Q And sitting here today, are they corrections that you would like to make with

respect to either of your declarations?
A I can't think of any.
Q Now, as far as your work in this case, you had a meeting with Dr. Goldberg, right?
A That's correct.
Q And that's Dr. Richard Goldberg, one of the declarants for JHU, in this case, right?
A He's a declarant, I don't recall his first name.
Q Was your meeting with Dr. Goldberg in person?
A No.
Q How did it occur, was it by phone?
A It was a Zoom call.
Q Zoom call.
And how long was your meeting with Dr. Goldberg?
A It was relatively short. I don't remember the exact time, on the order of 30 minutes. Could have been longer.
Q You said relatively short, so how much beyond 30 minutes in your view is relatively

short?
A It would have been an hour or less but my recollection was that it was less than an hour, that's my recollection.
Q Okay. And other than yourself and Dr. Goldberg, did anyone else attend this meeting?
A Yes.
Q Who attended the meeting?
A Attorneys for Hopkins.
Q Anyone else attend the meeting?
A No.
Q And what did you discuss with Dr. Goldberg during this meeting?
A It's the first time that I had ever met him so there was a little bit of meet and greet and then we discussed some aspects of his declaration, including his analysis of the relevance of the claims with respect to practicing the therapies that are described in the packages for pembrolizumab.
Q And you said you reviewed his

declaration, so when did this meeting occur?
A I don't recall the exact time, it was several months ago I think. I was in Michigan at the time so I should be able to figure that out.
Q Did this meeting occur before or after you signed your declaration?
A I don't recall.
Q And you said you talked about his declaration, did you have a copy of Dr. Goldberg's declaration at the time of this meeting?
A I don't recall.
Q How did you talk about the declaration?
A We talked specifically about the relevance of the claims in the '393 Patent to therapies described in the package insert for pembrolizumab.
Q Right. And you say at the time of the meeting you were in the Michigan, so how would you determine when the meeting actually occurred?

A The fastest way would be to look on my phone and look in my photos and look for photos from Holland, Michigan.
Q Do you have your phone nearby that you can do that?
A Yes. I can do that.
Q That would be great if you can please review your phone and let me know when you believe this meeting occurred with Dr. Goldberg?
A It would have been the first week of October from my memory.
Q Do you have a better date than that, the first week of October?
A We arrived in Michigan on October 3rd, so it would have been after October 3rd.
Q Do you know if it was October 4th, or 5th or beyond?
A No. I don't recall.
Q And you say when you met with Dr. Goldberg you say that you reviewed his declaration, right?

A I don't recall. We discussed the declaration. I don't recall the order in which I reviewed the declaration and the -- or which parts of the declaration and the phone call or the Zoom call, no, I don't.
Q Well, when you said that you reviewed his declaration, did you review it in its entirety or did you only look at parts?
A I don't recall.
Q Did you review the declarations of any other JHU declarants?
A I'm trying to recall. I believe that I reviewed the declarations of Dr. Pardoll and Dr. Le, and I -- there may have been others. I'm just -- don't recall right now offhand.
Q Okay. But you're confident that you reviewed the declarations by Dr. Pardoll and is Dr. Le, right?
A That is correct.
Q And was there just one meeting with Dr. Goldberg or were there multiple meetings that you had?

A Just that one meeting.
Q Okay. So in this case did you ever speak with Jennifer Newberger?
A Jennifer Newberger, no.
Q And you did not ever speak with Brian Segers, right?
A No.
Q As part as your work in this matter, did you have any meetings or discussions with any other JHU consultants or experts?
A No. I have only spoken to the JHU attorneys from Fish & Richardson about this case.
Q And as part of your work in this case, you didn't speak with Dr. Le, right?
A No. I haven't spoken to --
Q As part of your work --
A I haven't spoken to Dr. Le in over ten years.
Q And as part of your work in this matter, you didn't ever speak with anyone employed by JHU, right?

MR. MILLER: Objection. Form.
A It depends a little bit on how you define "as part of the work." In order -- my engagement in this case began with Dr. Pardoll reaching out to me and asking me if I would be willing to speak to the attorneys from Fish & Richardson.
Q Okay. So Dr. Pardoll called you directly?
A He either called me or texted me. I don't recall. He might have texted me and asked if I had time to speak.
Q Okay. And would you say that you and Dr. Pardoll are friendly?
A Yes. I've known him for many years.
Q As part of your work on this case, what did Dr. Pardoll tell you?
A I don't recall him telling me anything other than would I be willing to speak to the attorneys.
Q So all he said was there's some attorneys and would you be willing to speak

with them; is that your testimony?
A That's my testimony.
Q Okay. Did you speak with any other named inventor as part of your work on this case?
A No.
Q And other than the lawyers at the Fish & Richardson law firm, did you speak with any other attorneys in connection with your work on this matter?
A No.
Q Well, have you ever spoken with Mr. Matt Pearson from the Akin Gump law firm who's virtually with us today?
A That was not in relationship to this case other than whether or not he could be present to -- to represent Bristol Myers and protect Bristol Myers trade secrets and confidential information. But we've never discussed --
Q And so you don't think Mr. Pearson's reaching out about participating in this

deposition was anything related to this case? Is that your testimony?

MR. MILLER: Objection to form.

Go ahead.

A I do not believe so.

Q Okay. Did you speak with any in-house counsel at Bristol Myers as part of your work in this case?

A No.

Q Now, do you still have a copy of the posted study record, Exhibit 1005?

A Yes.

Q Okay. And would you agree that at the time of the posting of the study record, MSI-High testing was already standardized and performed in CLIA-certified laboratories without the need for assay development?

A That's correct, and that's why the design of this trial, to a person of ordinary skill in the art, would have looked like a biomarker trial in retrospective analysis. Because otherwise, there would have been no

point to Arm 2.
Q And would you agree that at the time the study record was posted, a reasonable anticipated outcome of the study was that there would be a greater number of clinical responses in the MSI patient group than the MS stable patient group?
MR. MILLER: Objection. Form.
A No. That was -- that's one of the hypotheses that's being tested in the trial. There's no expected outcome. If there was an expected outcome, I would not have included Arm 2 if I was designing this trial.
Q Okay. So I want to make sure you're understanding me. I didn't say "expected outcome"; I said "reasonable anticipated outcome." So let me try my question again.
Would you agree that at the time of the study record, posting a reasonable anticipated outcome of the study was that there will be a greater number of clinical responses in the MSI patient group than the

MSS group?
A I don't think so. I mean, you can go to the literature, Walter Bodmer's paper, the Nature paper. He specifically says in that paper that he doesn't think that immunotherapy would work in MSI positive patients.
Q And so is it your opinion that at the time of the study record's posting, it would have been unreasonable to anticipate an outcome of having a greater number of clinical responses in the MSI patient group than the MSS group?
MR. MILLER: Objection. Form.
A I think that it would have been reasonable to expect that there would be no responses or very few responses in the MSI-negative colorectal cancer patients, so I don't know what you mean by "fewer." But basically this is a hypothesis-testing clinical trial. There is no reason to anticipate a result prior to a

hypothesis-testing trial.
Q Okay. And I'm not sure if something's wrong with the audio because I never said the word "fewer," so let me try my question again.
Would you agree -- let me start over.
Do you think it would have been unreasonable at the time of the study record's posting to anticipate an outcome of having a greater number of clinical responses in the MSI patient group than the MSS group?
MR. MILLER: Objection. Form. Asked and answered.
A Isn't "fewer" in the positive the same as "greater" in the negative? I'm not sure I understand your misunderstanding.
Q Do you understand my question, Doctor?
A I don't understand the basis for your question, given that I already answered it.
Q Okay. Let me try it again. And you may never understand the basis for my question, just to be clear on that. I just have to ask

questions, and you can provide responses. So let me try this again.

Do you think that it would have been unreasonable at the time of the study record's posting to reasonably anticipate an outcome that there would be a greater number of clinical responses in the MSI patient group than the MSS group?

MR. MILLER: Objection. Form. Asked and answered.

A I think it would unreasonable to anticipate a particular outcome. That's not why you do a clinical trial. You do a clinical trial to test a hypothesis. You don't anticipate a particular outcome.

If you anticipated a particular outcome and you wanted to just see whether or not the number of responses was high enough to get a particular approval with a particular number of patients in a pivotal trial, you would not have done Arm 2. There's no reason to do Arm 2 if you had anticipated an answer.

Q Would you agree that at the time of the study record's posting on clinicaltrials.gov part of the rationale for doing such a study was that BMS's PD-1-blocking antibody nivolumab showed activity in melanoma?

MR. MILLER: Objection. Form.

A It was known that nivolumab and pembrolizumab were active drugs, and that is an obvious motivation for doing exploratory trial in different subsets of patients, different populations of patients.

Q Okay. I just want to be sure we're clear, would you agree that at the time of the MSI-High study record's posting on clinicaltrials.gov, part of the rationale for doing such a study was that BMS's PD-1-blocking antibody nivolumab showed activity in melanoma?

MR. MILLER: Objection. Form.

A It showed activity in melanoma and in other cancer types.

Q Okay. And I just want to -- I'm asking

a question about the rationale, so let me try it again, make sure we're on the same page.

Would you agree that at the time of the study record's posting part of the rationale for doing such a study was that BMS's PD-1-blocking antibody nivolumab showed activity in melanoma?

MR. MILLER: Objection. Form. Asked and answered.

A Part, yes. You used the word "part" in your question. Because it was also known to be active in other cancer types.

Q Understood. And so you would agree that at the time of the study record's posting part of the rationale for doing such a study was that BMS's PD-1-blocking antibody nivolumab showed activity in non-small cell lung cancer, right?

A Correct.

Q And you would agree that at the time of the MSI-High study record's posting part of the rationale for doing such a study was that

BMS's PD-1-blocking antibody nivolumab had a complete response in a single patient with colorectal cancer, right?
A That's correct.
Q And that complete response in that single patient was a MSI-High colorectal cancer patient, right?
A I don't know when that became public. And so when that would have been accessible to a person of skill in the art, but yes, it turned out that that person was MSI-High.
Q Okay. And you would agree that pembrolizumab and nivolumab have the same mechanism, right?
A That's correct.
Q And a POSA would have known that at the time of the study record's posting on clinicaltrials.gov, right?
A That's correct.
Q And you would agree that at the time of the study record's posting preclinical studies suggested that pembrolizumab and

nivolumab have a similar potency, right?
A That's correct.
Q And the person of ordinary skill in the art would have known that at the time of the study record's posting on clinicaltrials.gov, right?
A That is correct.
Q And you would agree that at the time of the study record's posting PK, or pharmacokinetic modeling suggested that pembrolizumab and nivolumab have similar pharmacokinetics, right?
A That's correct.
Q And the POSA would have known that at the time of the study record's posting, right?
A That is correct.
Q Now, would you agree with me that by the time of the critical date, there were publications discussing the clinical relevance of microsatellite instability in colorectal cancer, right?

A I'm sorry. Can you refer me to a particular paper?
Q I'm not asking about a particular paper right now.
My question is would you agree with me that by the time of the critical date, July 10, 2015, there were publications discussing the clinical relevance of microsatellite instability in colorectal cancer patients?
A That's correct, yes.
Q As part of your work on this case, you read a 2010 article by Chapelle, right?
A It sounds familiar. Can I look at my declaration to look at it? Do you remember what the exhibit number was?
Q The exhibit number is 1007.
(Whereupon, "Clinical Relevance of Microsatellite Instability in Colorectal Cancer," published 7-10-10 was marked as Exhibit 1007 for identification as of

this date.)
Q And we can put that in the chat so you can take a look at it if it helps.
A Yes. I read Chapelle.
Q Okay. And when you read Chapelle, you read it objectively, right?
A That's correct.
Q You didn't add any bias to your read of Chapelle, right?
A No.
Q And you read it from the perspective of how the person of ordinary skill in the art would read it, right?
A That's correct.
Q And you would agree with Chapelle -- let me start that again.
You would agree with the Chapelle group's assessment that by the publication date of their article it had been relatively well established that the prognosis is better for patients with MSI-High colorectal cancers, right?

MR. MILLER: Objection. Form.
A There may have been -- and I don't recall the particular papers, but there may have been other papers that came to a different conclusion.
Q Okay. And I wasn't asking you about if there were other papers that had a different conclusion. I'm asking about your belief and your understanding, so let me try the question again.
You would agree with the Chapelle group's assessment that by the publication date of their article it had been relatively well established that the prognosis is better for patients with MSI-High colorectal cancer, right?
A I would have to go back and look at the literature to make sure that I was making the correct assessment for person of skill in the art at the date, the critical date.
Q Okay. Let me try my question again 'cause I'm not sure why you referred to the

critical date when my question dealt with the publication date of the Chapelle group's article, and that was in 2010. So let me try my question again.

Would you agree with me -- or strike that.

Would you agree with the Chapelle group's assessment that by the publication date of their article, it had been relatively well established that the prognosis is better for patients with MSI-High colorectal cancer?

A I would have to go back and review the literature specifically to understand that publication date, what the understanding was at that publication date.

Q Okay. Well, you would agree that the POSA reading Chapelle would understand that the Chapelle group believed at the time of their publication it had been relatively well established that the prognosis is better for patients with MSI-High colorectal cancer, right?

A I don't know that the person of skill in the art would have accepted that.
Q Okay. I'm going to try my question again because my question wasn't about whether or not the POSA would accept something or not. My question was very specific, and it was about the belief of the Chapelle group. So let me try that again.
Would you agree that the POSA reading the Chapelle paper would understand that the Chapelle group believed at the time of their publication it had been relatively well established that the prognosis is better for patients with MSI-High colorectal cancer?
A I'd have to go back and read the language, the exact language in the Chapelle paper.
Q Let's take a look at it. If you can take a look at Exhibit 1007 and turn your attention to Page 6.
Let me know when you have it.
A Okay. I have it. What page?

Q Page 6.
A Page 6. It starts on Page 33180.
Q There should be a page for the exhibit number. Maybe look in the bottom left of the document.
A I'm there. You're referring to Page 3385.
Q I am. Thank you so much.
And you see on that page, exhibit Page 6, article Page 3385, there's a section entitled "MSI and colorectal treatment"?
A Yes.
Q And my question is, would you agree that the person of ordinary skill in the art looking at the Chapelle paper would understand that the Chapelle Group believed, at the time of their publication in 2010, it had been relatively well established that the prognosis is better for patients with MSI-High colorectal cancer?
A That prognosis -- it's interesting the way they used the word "prognosis," because

it's independent of therapy, of standard therapy, because there's a complication of what is the prognosis given standard therapy.

And so I think it's a little bit complicated. They're referring here to what I was referring to, which is that it wasn't a completely settled field at the time because they're referring to lack of control group in a particular paper, things like that. And then there was quite a bit of preclinical data on the affect of MSI-High on the sensitivity of the cancer cells themselves to find a few. So I think it was a little bit of a complicated area at the time.

Q Okay. Let me ask my question again.

Would you agree that the person of ordinary skill in the art reading the Chapelle paper would understand that the Chapelle Group believed in 2010 that it had been relatively well established that the prognosis is better for patients with MSI-High colorectal cancer as they write in

their paper?

MR. MILLER: Objection. Asked and answered.

A Yeah. But it's part of a longer sentence where they're sort throwing that out, and then they're saying, but it's a little more complicated because they're talking about prognosis, an underlying prognosis in the absence of therapy. Then they bring up the complication of outcome for chemotherapy.

Q Well, the remainder of the sentence reads whether or not MSI status predicts response to adjuvant chemotherapy has been more controversial, right?

A Exactly. That's going to be layered on to an actual prognosis if you've got a population of patients that has been treated with adjuvant chemotherapy. And so I --

Q And Dr. --

A Sorry. I think --

Q I'm only asking --

MR. MILLER: Preston, you're interrupting him. Let him finish his answer before you ask your next question.

MR. RATLIFF: But I don't think you understand my question.

MR. MILLER: It doesn't matter. Let him answer, then you can ask another question or clarify.

A I think Chapelle is recognizing how complicated this area is.

Q Let's go back to my question.

Do you see that the remaining part of the sentence states whether or not MSI status predicts response to adjuvant chemotherapy has been more controversial.

Do you see that?

A Yes.

Q And you would agree that the person of ordinary skill in the art would see that, right?

A Yes.

Q And pembrolizumab is not adjuvant chemotherapy, right?
A That is correct.
Q Now, would you agree that Chapelle recommends screening all colorectal cancer tumors for MSI status?
A My recollection of this paper was -- and other papers at the time, was that this was a call to test colorectal cancer patients because if it turned out that they were MSI-High, there's also a higher possibility, higher probability that there was an underlying Lynch syndrome. And that is something that the physicians should definitely be alerted to, because if they have Lynch syndrome, then even if you cure them of their colorectal cancer, they're likely to come up with another tumor.
Q And, Doctor, I was only asking about Chapelle. I just wanted you to understand that. My question is just about the Chapelle paper.

A Well, I would have to read the Chapelle paper carefully, but my memory is that the Chapelle paper was one of those papers at the time that was calling on people to test for MSI-High, so then they could do a subsequent test for Lynch syndrome.
Q And does your memory tell you, sitting here today, that Chapelle recommended screening all colorectal cancer tumors for MSI-High status?
A That is my memory. But, again, I would have to reread the paper.
Q Okay. And do you understand that the Chapelle paper, at the time it was published, explained to the public that an immunohistochemistry test was replacing MSI as a screening method for detecting MMR, right?
A Well, it was replacing the earlier PCR assay which looked at the size of the microsatellite repeat regions, and they're specifically amplified by PCR so that you can

look at the size, using gel electrophoresis.

Then a much easier to assay to perform with the immunohistochemistry assay which looked at specific enzymes associated with DNA mismatch repair. And then the subsequent innovation of direct DNA sequencing of the tumor.

Q And the POSA would know that by the time of the July 10, 2015 critical date, right?

A That's correct.

Q Now, as part of your work on this case, you read a 2014 publication by Salipante, right?

A That sounds familiar.

Q And that publication was all about microsatellite instability detection by next generation sequencing, right?

A I'd have to look at it, but that sounds familiar.

Q Okay. And do you remember, when you read Salipante, did you read it objectively?

A Yes.

Q You didn't have any bias to your read of Salipante, right?
A No.
Q And would you agree that the person of ordinary skill in the art would understand that Salipante's group had an assessment at the time of their publication that it had been established that MSI-High is a useful phenotype in cancer diagnosis and prognosis, right?
A That is my recollection. But, again, I don't have the paper in front of me.
Q Okay. And would you agree that the POSA would understand from Salipante Group, that by the time of their publication, diagnosis of MSI often had important clinical implication, including informing therapeutic choices, cancer prognosis and familiar cancer risk, right?
A I think the latter two are well established, and the therapeutic choices was less well established.

Q But the POSA would understand that with the assessment of the Salipante Group, right?
A I'd have to go back and look at the Salipante paper.
Q We can take a look at the paper. Let's bring up Exhibit 1010.

(Whereupon, "Microsatellite Instability Detection by Next Generation Sequencing," published September 2014 was marked as Exhibit 1010 for identification as of this date.)

Q You can let me know when you have it.
A Okay. I have the paper.
Q Do you recall reading this paper as part of your work on this case?
A Yes.
Q And can you turn your attention to Exhibit No. 4, Exhibit page number four, it should be at the bottom of the document.
A Yes.
Q And do you see where the writers of this

publication begin to write:

"Diagnosis of MSI-High often has important clinical implications"?

A Where is that on the page? I see it.

Okay. So they have references five through seven. So I'd have to go and look at -- I'd have to go and look at references five through seven to see whether or not I would agree with that. I've lost the --

Yeah. I'd have to go back and look at those references.

Q Okay. I don't think you understand my question.

So my question is not whether or not -- let me just try my question.

Would you agree that the person of ordinary skill in the art, looking at the Salipante Group papers, would understand that the Salipante Group had stated publicly, diagnosis of MSI often has important clinical implications in forming therapeutic choices, cancer prognosis and familiar cancer risk

appraisal?
A Well, the authors of this paper are experts at developing diagnostics. And so I'm not sure that a person skilled in the art would take it face value a conclusion like that.
Q So, in your view, the person of ordinary skill in the art would do an assessment of who are the writers of the publication --
A No.
Q -- and come to a -- I wasn't finished with my question.
Is it your testimony that the person of ordinary skill in the art, reviewing the prior art, would do an assessment of the writers of the prior art and make a determination whether or not they are qualified to make the statements that they make in those pieces of prior art?
A Is that it?
MR. MILLER: Objection, form.
Q Yes. Is that a step you believe that

the person of ordinary skill in the art would take?

MR. MILLER: Objection, form.

A I believe that a person of ordinary skill in the art would not take that statement at face value. And that they would understand that there's a little bit of promotion, it goes on in that paper, particularly a paper about a new diagnostic. So that sentence looks a little bit promotional.

So, anyway, they would read carefully references five through seven, reference one, reference two, reference eight through ten.

Q So I understand you have positions, Doctor, but my question was different. It actually wasn't about this particular paper. It was broader. So let me go back to my question.

Do you believe that the person of ordinary skill in the art would take the step for any prior art reference they read of

making a determination of whether or not the writers of that prior art had the necessary background to make the statement in the prior art that's before the POSA?

MR. MILLER: Objection, form.

Q Is that a step that you think the POSA can make?

A There is this sort of invocation of authority that you see sometimes in the scientific community. And it is an incorrect attitude. I don't remember the Latin phrase that is the motto of the British scientific society, but it pokes fun at that.

I don't think that a good scientist, and certainly not a person of skill in the art, would believe that the invocation of authority. I think you roll down and you look at the data. And so that's why you read papers five through seven, paper one, paper two, and papers eight through ten. You don't just rely on invocation of authority.

Q Okay. But would you agree that the

person of ordinary skill in the art, looking at the Salipante Group's paper, would believe that the Salipante Group is of the opinion that diagnosis of MSI often has important clinical implications in forming therapeutic choices, cancer prognosis and familial cancer risk appraisal?

MR. MILLER: Objection, form.

A A person of skill in the art would have thought that that was irrelevant what the Salipante Group thought.

Q But I'm not asking if they -- what the person of ordinary skill in the art would have thought was relevant or irrelevant. I'm asking you a different question.

Do you believe that the person of skill in the art, looking at the Salipante paper, would believe that the Salipante Group were of the opinion that diagnosis of MSI often has important clinical implications, informing therapeutic choices, cancer prognosis and familiar cancer risk appraisal?

MR. MILLER: Objection, form.
A I don't think that's a determination that requires a person of ordinary skill in the art. I think even a lawyer could read that and say that's the plain English in this piece of paper.
Q And do you understand that the Salipante paper explains that evaluation of the MSI phenotype by next-generation sequencing is valuable?
A I'm sorry. Could you repeat the question.
Q Do you understand that Salipante explains that evaluating MSI phenotypes by next-generation sequencing is valuable?
A Yes. That's what is stated in the paper, and it's also what I think a person of ordinary skill in the art would have thought.
MR. MILLER: Preston, are you close to closing out on this referent?
MR. RATLIFF: I am not.
MR. MILLER: All right. We've been

going well over an hour, and we're getting to lunchtime here. We would like to take a break.

MR. RATLIFF: Dr. Lonberg, would you like to break for lunch?

THE WITNESS: Yes --

MR. RATLIFF: Or just take a break?

THE WITNESS: Yes, please. Take a break for lunch.

MR. RATLIFF: Okay. It's almost 1:00 p.m. Pacific?

MR. MILLER: Correct.

MR. RATLIFF: How does half an hour sound or 45 minutes? What works for you, Doctor?

MR. MILLER: Somewhere between 30 and 45.

MR. RATLIFF: Okay. Sounds good.

(Whereupon, a recess was taken from 3:59 PM until 4:41 PM.)

Q Doctor, do you have a copy of the '393 Patent in front of you?

A Yes, I do.
Q And can you just turn to the first page of that patent. And you see a list of named inventors on that page, right?
A Yes.
Q Can you identify any of the named inventors that you have a personal relationship with?
MR. MILLER: Objection. Form.
A Drew Pardoll and Suzanne Topalian are friends.
Q Okay. And have you spoken to Dr. Topalian at all in connection with your work on this case?
A No.
Q Now, Doctor, would you agree that before the critical date, July 10, 2015, that there were publications stating that colorectal cancer associated with MSI could lead to a more intense immune response, making such patients good candidates for immunotherapy?
A There is a paper that you may be

referring to. Was it Pernot? Is that the paper you're referring to?

Q I'm not referring to any particular paper. I'm asking you would you agree that before the critical date that there were publications stating that colorectal cancer associated MSI could lead to a more intense immune response, making such patients good candidates for immunotherapy?

A Yeah, I believe -- well, Pernot is prior to the critical date. I believe Pernot has language like that.

Can I pull Pernot up? Can we pull it up so that I can point you to the language that I think you're referring to?

Q Sure. Let's take a look at -- I believe Pernot is Exhibit 1006.

(Whereupon, "Colorectal cancer and immunity," published 4-14-14 was marked as Exhibit 1006 for identification as of this date.)

TECH WELCH: 1006 is uploading now.

Q Just let me know when you have Pernot, Doctor.
A Yes. It'll take a minute to find what your referring to. I'll be there in a minute. Just...
Q Did you find it, Doctor?
A Yeah, I'm still looking. It'll just take me a minute.
Q What question are you trying to answer?
A Well, there was a particular passage. My memory is that it was Pernot where they talk about the potential for immunotherapy in MSI-High colorectal, so.
Q Okay. Maybe I can direct your attention, since we're looking at Pernot, to exhibit Page 5 of Pernot, which is Exhibit 1006.
And do you see -- I think there's a portion in Pernot where there's a sentence beginning "Altogether, CRC associated with"?
A Yeah, and that's -- I thought that was interesting. I thought that was really the

main point of this paper because they're talking about -- you'll see that leading up to that sentence, the "altogether" sentence, is a discussion of specific mechanisms by which MSI-High tumors evade the immune system.

And there's two particular mechanisms they call out. One is the high density of intratumoral regulatory T cells, and the other is the lower expression of HLA.

And so then what that sentence "altogether" is referring to is that when they say "specific immunoregulatory phenomenon" is that if you had drugs that could target the specific immune evasion mechanisms, that would be an interesting path for immunotherapy.

And so if you had, for example, a drug like ipilimumab that depletes regulatory T cells or perhaps a cytokine therapy that induces HLA class II -- although they don't discuss HLA class II, which could compensate

for lower HLA class I. That if you had drugs like that, that might be interesting because you've already got a tumor that is selected for dependence on those particular mechanisms.

PD-1 blockade is not a mechanism like that, so I don't read this as having anything to do with PD-1 blockade.

Q Do you know what was my question that I asked you?

A If you want to repeat your question, that would be great.

Q Now, I'm just asking do you know what my question was. I don't want to repeat it. Of course I don't want to waste time to repeat it.

Do you know what I asked you?

A I would like you to repeat it.

Q It's not helpful for me to repeat. I just want to make sure -- I'm trying to be mindful of your time, and if we're not understanding the questions, then I'm just

trying to make sure we appreciate that. But let me try my question again.

Do you agree that before the critical date, July 10, 2015, there were publications stating that colorectal cancer associated with MSI could lead to a more intense immune response, making such patients good candidates for immunotherapy?

A That's almost exactly what's written right on Page 5 in the sentence that you directed me to. But I don't think that immunotherapy in this case is referring to PD-1 blockade.

Q Okay. And would you agree that the POSA would have seen in the Pernot article -- and this is Exhibit 1006 -- specific mention of molecules called "immune checkpoints"?

A Yeah. That was mentioned almost in passing. Let me see if I can pull that up. Under other escape mechanisms are suspected in CRC, B7H1 or PDL-1 --

MR. MILLER: You're going to have to

go slower if you're going to read.

THE WITNESS: Oh. Sorry.

A So this is on Page 3742:

"Recently some monoclonal antibodies targeting these molecules (PD1, CTLA-4) have shown more than promising efficacy results in solid neoplasia such as melanoma and others."

Q Okay. Are you ready to answer my question?

A Do you want to repeat your question?

Q Sure.

Would you agree that the POSA looking at the Pernot article would have seen a specific mention of molecules called "immune checkpoints"?

A I don't doubt that is in here but -- oh, there it is. Yes. I agree, yes.

Q Okay. And you would have seen -- would you agree that the POSA would have seen that the Pernot article specifically references the immune checkpoint inhibitors ipilimumab

and nivolumab, right?
A I see where it says "some monoclonal antibodies targeting these molecules." I don't see the words "ipilimumab" and "nivolumab" right now, but I'm assuming that that's what's referenced in References 58 through 60.
Q Okay. And you can take a look at the references. So you can go towards the end of the article. You'll see the references for 58 through 60, right?
A Yes. 58 is ipilimumab. 59 is the combination of nivolumab plus ipilimumab. And 60 is pembrolizumab.
Q Okay. And so the POSA would have seen in Pernot a specific reference to the checkpoint inhibitors ipilimumab, nivolumab and pembrolizumab; right?
A That's correct.
Q And nivolumab is the checkpoint inhibitor that was posted on clinicaltrials.gov for a clinical trial in

MSI-High patients before JHU even applied for the patent at issue in this case, right?
A My memory is that that trial was an exploratory trial of a set of rare diseases, and one of those rare diseases was MSI-High cancer.
Q Okay. So let me try my question again.
Would you agree that nivolumab is the checkpoint inhibitor that was posted on clinicaltrials.gov for a clinical trial in MSI-High patients before JHU even applied for the patent at issue in this case?
A Well, I don't have that in front of me, so I don't recall the dates.
Q Okay. Do you recall the dates when JHU applied for a patent in this case?
A The first priority date, is that what you're asking for?
Q Yeah.
A Was the first priority date? I don't recall the exact date. My memory is it's in 2013.

Q You have your declaration in front of you, right?
A I have it, yes.
Q Can you turn to Paragraph 8 of your declaration. And then can you read that to yourself and let me know when you're finished.
A Yes. Finished.
Q Okay. And does that refresh your recollection as to when JHU first applied for the patent at issue in this case?
A Yes.
Q And that date was November 13, 2014; is that right?
A That's correct.
Q Okay. Let me turn your attention to an exhibit. It's Exhibit 1053.

(Whereupon, Study NCT02060188, dated 2-10-14 was marked as Exhibit 1053 for identification as of this date.)

Q We can put that in the chat, and you can

take a look at it.

TECH WELCH: 1053 uploading now. It may be just a moment.

A Yes.

Q Okay. Now, you see that Exhibit 1053 is a study record for nivolumab?

A Yes.

Q And do you see that Exhibit 1053 is the February 10, 2014 version of that study record?

A Yes.

Q And so would you agree with me that nivolumab is the checkpoint inhibitor that was posted on clinicaltrials.gov for a clinical trial in MSI-High patients before JHU even applied for the patent at issue in this case?

MR. MILLER: Objection. Scope.

A Yes.

Q And before the critical date, July 10, 2015, pembrolizumab was publicly known to be an immunotherapeutic, right?

A Yes.
Q And before the critical date, pembrolizumab was publicly known to be a checkpoint inhibitor, right?
A Yes.
Q Would you agree with me that before the time of the critical date, July 10, 2015, there were publications that discussed the treatment of colorectal cancer patients in clinical trials?
A I'm sorry. Could you repeat the question?
Q Sure.
Would you agree with me that before the critical date there were publications that discussed the treatment of colorectal cancer patients in clinical trials?
A Yes.
Q And would you agree that the Benson publication that you read in this case was about colorectal cancer patients?
A The Benson publication. Can you remind

what the Benson publication is?
Q Sitting here right now, you don't remember Benson?
A It sounds familiar, but I don't remember which particular paper Benson was.
Q Okay. Let's take a look at Exhibit 1009.
TECH WELCH: 1009 is uploading now.
(Whereupon, "Colon Cancer, Version 3.2014, Clinical Practice Guidelines in Oncology," published July 2014 was marked as Exhibit 1009 for identification as of this date.)
Q Just let me know when you have the exhibit, sir.
A Yes, I have it.
Q And this is the publication that you read as part of your work in this case?
A Yes.
Q Okay. And would you agree that the Benson publication that you read as part of

your work in this case was about colorectal cancer patients?
A Yes.
Q And the publication was specifically about clinical practice guidelines, right?
A That is correct.
Q Now, when you read the Benson publication, you read it objectively, right?
A Yes.
Q You didn't add any bias to your read of Benson, right?
A No.
Q And you understand that Benson gave a summary of the then in place national comprehensive cancer network clinical practice guidelines in oncology for managing metastatic colorectal cancer, right?
A Yes.
Q And Benson explains that the guidelines are believed to represent the optimal treatment strategy, right?
A Yes.

Q And you agree that the then NCC guidelines recommended including clinical studies as a therapy for metastatic cancer patients who had a third progression or more of their cancer, right?
A I don't recall that.
Do you want me to the find it?
Q Sure.
A Do you want to point me to the language?
Q Well, I'm asking the question, but you can turn your attention to Page 7 of the exhibit to see if it's helpful to responding to my question.
A Yes.
Q "Yes" is the answer to my question?
A Yes. Regorafenib, if not given previously or clinical trial or best supportive care.
Q Now, before the critical date, July 10, 2015, you would agree with me that pembrolizumab was administered to patients intravenously, right?

A Yes.
Q And before the critical date, you agree that there were publications that discuss intravenous administration of pembrolizumab, right?
A Yes.
Q And one of those publications that you read as part of this case was a 2013 article by Hamid, right?
A Yes.
Q And when you read the Hamid article, you read it objectively, right?
A Yes.
Q You didn't try to add any bias into your reading of Hamid, right?
A No.
Q You understand that the Hamid Group was providing to the public results of a clinical study of pembrolizumab in patients with measurable metastatic or locally advanced unresectable melanoma, right?
A That's my memory.

Q You would agree with the Hamid Group's assessment that their clinical study confirms the importance of releasing inhibitory immune regulations by PD-1 for respective antitumor immunity, right?
A I don't recall the language.
Q Let's take a look. Why don't you take a look at Page 10 of Hamid, and we can bring it up if you don't have the exhibits.
Exhibit 1011.
Just like the other exhibits, Doctor, let me know when you have it.
A Yes. I have it.
Q Can you turn your attention to Page 10?
(Whereupon, "Safety and Tumor Responses with Lambrolizumab (Anti-PD-1) in Melanoma," published 7-11-13 was marked as Exhibit 1011 for identification as of this date.)
A Okay. I'm on Page 10.
Q Do you see on Page 10 where the Hamid

authors write about what their study confirms?
A Yes.
Q And you would agree with the Hamid Group's assessment that their clinical study confirms the importance of releasing inhibitory immune regulation by PD-1 for respective antitumor immunity, right?
A That's correct.
Q That would have been knowledge of the person of ordinary skill in the art at the time the study record was posted, right?
A That is correct.
Q You understand that the Hamid Group explained to the public that they administered pembrolizumab to patients intravenously, right?
A That is correct.
Q You understand that the Hamid Group explained to the public that they administered pembrolizumab at a dose of 10-milligrams per kilogram every two or

three weeks, right?
A I know it was 10-milligrams per kilograms for two or three weeks. Yes, they compared, two weeks versus three weeks.
Q Okay. And the POSA at the time of the posting of the study record would have seen in the Hamid article the specific mention of administering pembrolizumab intravenously, right?
Let me try that again. Tongue twister.
You would agree that the POSA, at the time of the posting of the study record, would have seen in the Hamid article the specific mention of administering pembrolizumab intravenously, right?
A That's correct.
Q Now, before the critical date, July 10, 2015, there were publications that concluded that high levels of mutational heterogeneity in a tumor could be the key for success of immune checkpoint targeting, right?
A I'm sorry. Can you just repeat that one

more time.
Q Sure. Would you agree that before the critical date, there were publications that concluded that high levels of mutational heterogeneity in a tumor could be the key for success of immune checkpoint targeting, right?
A I'm not sure if the word, or the phrase "the key" is accurate, but there were certainly papers that correlated tumor mutational burden with outcome for checkpoint blockade therapy.
Q Great. And maybe what we can do, we can look at an example, maybe if we can look at the Champiat 2014 publication that you read as part as your work in this case. So that's Exhibit 1032. If we can put that in the chat.
Just let me know when you have it.
(Whereupon, "Exomics and immunogenics: Bridging mutational load and immune

checkpoints efficacy," published January 2014 was marked as Exhibit 1032 for identification as of this date.)

A I have it.

Q So you recall reading the Champiat 2014 publication, right?

A Yes.

Q If I can turn your attention to the first page of this exhibit. And so you see where they formulate a hypothesis?

A At the very top of the page, on the right-hand column, "These observations may suggest that the mutational heterogeneity of the tumor could be the key of the success of immune checkpoint targeted therapy."

Q Right. And so this is a publication from 2014, right?

A That is correct.

Q So this is before the critical date in this case, right?

A That is correct.

Q Let me ask my question, just to make sure it's clear.

Before the critical date, there were publications that concluded that high levels of mutational heterogeneity in a tumor could be the key for success of immune checkpoint targeting, right?

MR. MILLER: Objection, form.

A This is not a conclusion, this is a hypothesis.

Q Right. So you -- okay. Well, you agree that before the critical date there were publications that were proposing that high levels of mutational heterogeneity in a tumor could be the key for success of immune checkpoint targeting, right?

A That was a hypothesis. And there are many hypotheses that turned out to be wrong, as I alluded to before the concept of depleting regulatory T cells for treating MSI-High tumors has not been proven.

Q Okay. Well, you would agree that the

POSA would have knowledge of the Champiat Group's observation of a significant association between mutational load of tumors and their susceptiblity to PD-1, PDL1 targeting agents, right?

MR. MILLER: Objection, form.

A You just mixed up two very different concepts. One is mutational load and the other one is mutational heterogeneity.

Q I don't think I did anything of the sort. So let me ask my question.

Would you agree that the person of ordinary skill would have knowledge of the Champiat Group's observation of a significant association between the mutational load of tumors and their susceptibility to PD-1, PDL1 targeting agents?

A The sentence here refers to observations by others. And then the Champiat Group is proposing hypothesis that suggests it's mutational heterogeneity and not mutational load.

Q What page are you looking at, Doctor, in the Champiat publication?
A The first page.
Q Now I think maybe why we're misunderstanding each other.
Can you turn to Page 3 of the Champiat exhibit.
A Yes. Figure three -- Figure one, I mean?
Q I'm talking about where the Champiat authors talk about what they observed. The bottom of the second column and going into the third column on that page.
A This is not their work, they're referring to the work by others, they use the passive of voice, they say are observed.
Q Do you see where they write "We observed a significant association"?
A You're talking about the middle paragraph?
Q I'm talking about the paragraph that's the bottom of the second column and going

into the third column.

A As a hypothesis generated case we observed a significant association between the mutational load of tumors and their -- okay. So they're observing basically based on data by others. And that's Figure 1. And I think Figure 1 is kind of key to explaining their hypothesis because it's not linear with -- the responses to checkpoint blockade are not linear with mutational load. And that's why kidney cell cancer stands out. And it's why DLBCL and ovarian and glioblastoma don't respond to checkpoint blockade. And they all have higher mutational load than RCC, and all much higher, RCC has much higher mutational load than, say, polyomavirus positive Merkel cell carcinoma. And yet polyomavirus positive Merkel cell carcinoma responds to checkpoint blockade.

So there's kind of this nonlinearity, and then they come up with hypothesis that I

think it's an interesting hypothesis, but it is just a hypothesis, that is that it's mutational heterogeneity.

Q And what question were you answering? I just want to make sure the record is clear.

A I was trying to explain what their observation referred to.

Q Okay. Okay. So my question is different.

Would you agree that the person of ordinary skill would have knowledge of the Champiat Group's observation of a significant association between mutational load of tumors and their susceptibility of PD-1, PDL1 targeting agent?

A Yeah. That's what's written in their paper, yes. And that is referring to Figure 1.

Q And the POSA would also understand --

A Figure 1 highlights the discordance. And that's the reason I think why they came up with this hypothesis of mutational

heterogeneity, and then they proposed testing that hypothesis.

Q Now, Doctor, would you also agree that the POSA would understand, at least from the Champiat paper, that DNA mismatch repair deficient tumors including MSI-High colorectal cancer displayed severe genomic instability?

A Yes.

Q Would you agree that Champiat recommends evaluating the clinical activity of PD-1, PDL2 agents in MSI-High colorectal cancer?

A Well, they have a sort of a step wise -- their sentences -- their proposal is kind of step wise. They propose basically testing their hypothesis about mutational heterogeneity, not mutational load, and that if that is correct, then it would be interesting to test checkpoint blockade in MSI-High patients.

Q Let me try my question again. I actually don't think it was framed in the

right way. So I want to help you.

Would you agree that Champiat recommends evaluating the clinical activity of PD-1, PDL-1 agents in MSI-High colorectal cancer?

A But there's a caveat in the paper, the actual sentence is moreover if high levels -- if high levels of mutational heterogeneity increase the tumor immunogenicity it will be interesting. So they are implicitly proposing testing that hypothesis and then if that hypothesis is true then it would be interesting to evaluate the clinical activity of PD-1, PDL-1 agents. In fact, shortly after the critical date there was a set of experiments that were done and an analysis from a group in the UK Swanton et al., where they showed, in fact, mutational heterogeneity was not the key. That, in fact, it was a requirement for successful checkpoint blockade therapy with clonal mutations and not heterogeneous mutations. So, in fact, the entire hypothesis of

Champiat was quickly shown to be incorrect.
Q Doctor, do you believe that art from after the critical date should be used as an assessment of whether or not the '393 Patent should be considered to be obvious?
MR. MILLER: Objection. Form.
A I did not say that. That was not part of my answer.
Q I didn't say you did. I'm just asking the question. So let me try it again.
Do you believe it is appropriate to rely upon a reference from after the critical date in making an assessment as to whether or not any of the claims of the '393 Patent are obvious?
A No. And that's why a person of skill in the art wouldn't have gone to Swanton because they couldn't go to Swanton, instead a person of skill in the art would have gone to a paper by the UCLA group, Antoni Ribas's group. Antoni Ribas was the senior author on the Hamid article that you brought up before

and that article preceded the critical date and that article they looked at T-cell clonality, essentially heterogeneity, during treatment, cross treatment with either ipilimumab or nivolumab, there may have been some pembrolizumab patients in there also. What they found was that the heterogeneity of the T-cell response did increase with ipilimumab therapy, but it did not increase with PD-1 blockade therapy. And that's consistent with what I think was understood at the time in the art, which was it's just as likely that it was not mutational antigenic heterogeneity that, in fact, it could be just dominant antigens. And there were examples, certainly in the preclinical mouse literature, Schreiber et al., where they found that there was single or two dominant antigens that were driving the immune response to a tumor in a mouse tumor model. And then there's also an example from the National Cancer Institute,

Dr. Rosenberg's group where they found that a clonal T-cell transfusion could drive an effective antitumor response in a patient.

Q Okay. So I understand you have positions, Doctor, but I just want an answer to my question.

Just to be clear. I asked you, do you believe it is appropriate to rely upon a reference from after the critical date in making an assessment as to whether or not any of the claims of the '393 Patent are obvious?

MR. MILLER: Objection. Form.

Q What's the answer to that question?

MR. MILLER: Objection. Asked and answered. Go ahead.

A No. And that's why I then came back with a set of articles that a person of ordinary skill in the art would be aware of that were prior art prior to the July 10, 2015 date.

Q Now, before the critical date, would you agree that there were publications stating

that PD-1, PDL-1 were differently expressed in molecular subtypes of colon cancer pointing to MSI-High and MSS cases?

MR. MILLER: Objection. Form.

A Yes.

Q Okay. From one of those publications was a 2014 article by Dr. Gatalica, right?

A I would have to go back and look at that.

Q Do you recall reading an article by Dr. Gatalica in this case?

A I -- it sounds familiar, but I would want to go back and make sure that I'm thinking of the right paper.

Q Okay. Would you agree that before the critical date there were publications stating the patients showing naturally immunogenetics mutation associated with tumor infiltrating lymphocytes are potential candidates for treatment with immune modulators such as PDCD-1 targeted antibody?

A That sounds correct, my recollection is

that that would have been in the literature, yes.

Q Okay. Would you agree that before the posting of the study record there were publications noting that MSI is a common molecular classifier of colon cancer, right?

A That's correct.

Q Now, would you agree that years before the posting of the MSI-High study records, there were publications describing that colorectal cancers with Microsatellite Instability are characterized by tumor infiltrating lymphocytes and have a good prognosis?

A Yes.

Q Now, before the posting of the study records you would agree that there were publications explaining the tumor infiltrating T-cells may be an indicator of post immune response to tumor and an attractive target for immunotherapy, right?

A Yes.

Q Now, would you agree that before the critical date there were publications that explain that there was a strong inflammatory response in MSI-High colorectal cancer patients triggering the expression of PDL-1, which can be targeted to enhance clinical benefit and be predictive of response to immune checkpoint inhibitors?
A I don't recall that specific language. Can you point me to the paper.
Q Sure. Why don't we look at an example. If we can bring up Exhibit 1039.
TECH WELCH: 1039 is uploading now.
Q Do you have Exhibit 1039?
A Yes. I'm just trying to get past the -- okay, yes, I'm there.
(Whereupon, Description of presentation "Immune checkpoints expression in MSI versus MSS colorectal cancers and their potential therapeutic implications" on 5-31-14 was

marked as Exhibit 1039 for identification as of this date.)

Q And do you recall reading Exhibit 1039 as part of your work on this case?

A Yes.

Q And this is the publication by Llosa; is that right?

A Yes, yes.

Q Okay. And would you agree that before the critical date, the Llosa Group were telling the public that a strong inflammatory response in MSI colorectal patients triggered the expression of PDL-1, which could be targeted to enhance clinical benefit and be predictive of response to immune checkpoint inhibitors?

A Yes. It actually says on PDL-1 and IDL-1.

Q It's both, right?

A Yes.

Q Your read of Llosa, as part of this case, you gave it an objective read, right?

A Yes.
Q You didn't add any bias to your read of Llosa, right?
A No.
Q Would you agree that prior to the critical date there were publications stating that tumors with a high level of mutations such as melanoma, non-small cell lung cancer, are deriving striking benefits with immune checkpoint blockage drugs?
A Yes. But I'm also aware of striking benefit in low tumor mutational burden tumors, and of no responses in higher mutational burden tumors, so I am.
Q Okay.
A I don't think someone of skill in the art would have at the time of the -- at the critical date would have been -- would have treated tumor mutational burden as a single key identifier of patients to be treated with checkpoint blockade as more than just a hypothesis.

Q And do you know what was the question I asked you?
A I'd like you to repeat it.
Q I just want to know do you know what I asked?
A I'd like you repeat it, make sure that I understood it.
Q Do you believe that you might understand it, I want to be efficient with your time, do you know what I asked you or not?
A I think the most efficient use of my time would be to repeat the question.
Q Let me ask a different question.
Would you agree that before the critical date July 10, 2015 there were publications stating that high levels of genomic instability may make immunotherapy particularly suitable as a therapy?
A I'd like to see the reference.
Q Well, I'm not talking about any particular reference. I'm asking you based upon your knowledge and experience, would you

agree that before the critical date there were publications stating that high levels of genomic instability may make immunotherapy particularly suitable as a therapy?
A Well, you gave very specific language. I know of papers that correlated immune responses to a level of mutational burden.
Q You know of those occurring from before the critical date?
A Yes.
Q Would you agree with me that prior to the critical date there were publications stating that MSI-High colorectal cancer patients may have greater responses to checkpoint blockade therapy?
A I would like to a particular reference because that's very specific language that you used, and I'd also like to see the context of where that language was used.
Q And sitting here today, right now, do you have any opinion one way or another whether prior to the critical date there were

publications stating that MSI-High colorectal cancer patients may have greater responses to checkpoint blockade therapy?

A Well, that's a very specific wording that you gave, and I don't have an opinion as to whether that particular sentence was out there in the literature, so I'd like to see what you're referring to.

Q Okay. And I wasn't referring to a particular sentence and I am trying to be precise in my question. So let me try it again.

Would you agree that prior to the critical date there were publications explaining that MSI-High colorectal cancer patients may have greater responses to checkpoint blockade therapy?

A You said may, so you're talking about with the hypothesis out there. Yes, the hypothesis is out there.

Q Now, before the July 10, 2015, critical date, you are aware that Dr. Gatalica that we

mentioned earlier, publicly reported that there were more than five PD-1, PDL-1 clinical trials were ongoing, do you recall that?

A I don't recall that part of the publication. Should I pull it up, again?

Q We can pull up Exhibit 1084.

(Whereupon, "Caris Life Sciences Research Provides Key Clinical Insights on Immunotherapeutic Targets in a Broad Range of Cancers," dated 6-10-14 was marked as Exhibit 1084 for identification as of this date.)

A Okay. I have it.

Q Do you recognize Exhibit 1084 as a document that you referred to in your October 4, 2024, declaration?

A I may have. I would have to look at my declaration to see if this is a document.

Q And sitting here today, right now, you just don't have a recollection of whether or

not you referred to Exhibit 1084 in your declaration?
A I don't want to -- I don't want to go beyond my recollection, which is why I'd like to see if this is the specific document.
Q And, sir, to be clear I'm not asking you to go beyond your recollection, I'm asking that very question. Sitting here right now, in this moment, do you have a recollection, one way or the other, if you actually refer to Exhibit 1084 in your October 4, 2024, declaration?
A I have a recollection, but it's not a specific recollection, and that's why I would like to make sure that this is the correct document.
Q Fair enough. Do you recall reviewing Exhibit 1084?
A I would like to -- it looks familiar, but I would like to make sure that this is the same document that I reviewed.
Q Do you have your October 4, 2024,

declaration in front of you?
A Yes.
Q Let me turn your attention to Page 80 of your declaration.
Do you see that you have a citation to Exhibit 1084?
A Oh, yes, yeah.
Q Does this refresh your recollection that you looked at Exhibit 1084?
A Yes. But I want to look for that particular language that will refresh my memory.
Q Which particular language are you looking for?
A The language in my declaration.
Q Let me know if you see it.
A Yes. I found it. That's -- that is the article that I reviewed, yes.
Q And when you reviewed it, you reviewed it carefully?
A Yes.
Q And would you agree that before the

July 10, 2015, critical date, Dr. Gatalica reports that there were more than five PD-1, PDL-1 clinical trials were ongoing?
A Yes.
Q And Dr. Gatalica publicly reported that his study produced similar findings to the Phase II MSI-High study that's referred to in the study record, right?
A I'm looking for that language.
His findings are similar to those from a Phase I study, PD-1 antibody patients with MSI tumors, yes.
Q Right. So Dr. Gatalica publicly reported that his study produced similar findings to the Phase II clinical trial that's described in the MSI-High study record, right?
A He says conducted at John Hopkins so I'm assuming, yes, that is the study record trial.
Q And you would agree that this Gatalica publication would have been knowledge that a

POSA would have had as of the time of the critical date, right?
A Correct.
Q Now, would you agree that by the time of the critical date, July 10, 2015, there was another clinical trial about administering an anti-PD-1 inhibitor to MSI-High colorectal cancer patients?
A Which trial are you referring to?
Q How about the trial involving nivolumab?
A Yes.
Q So you would agree that by the time of the clinical date there was another clinical trial about administering an anti-PD-1 inhibitor to MSI-High colorectal cancer patients, right?
A Correct.
Q And you would agree that there was a clinicaltrial.gov posting by the time of the critical date about that other clinical trial involving administration of an anti-PD-1 inhibitor to MSI-High colorectal cancer

patients, right?
A Correct.
Q And that nivolumab trial about administering an anti-PD-1 inhibitor to MSI-High cancer patients was sponsored by BMS, correct?
A That's correct.
Q BMS is that Bristol Myers Squibb, am I right?
A That's correct.
Q And at the time of the study records posting for this nivolumab trial involving a study of an anti-PD-1 inhibitor to MSI-High colorectal cancer patients, you were working at BMS, right?
A That's correct.
Q And you would agree that the purpose of this trial conducted by BMS was to examine if nivolumab alone or in combination with ipilimumab would demonstrate a meaningful objective response rate in patients with recurrent and metastatic colon cancer who

also have a specific biomarker in their tumors, right?

MR. MILLER: Objection. Form.

A Who also have a specific biomarker, is that what you said?

Q Who also have a specific biomarker in their tumors?

A A biomarker beyond MSI-High.

Q Let me try my question again.

A Can we go to that study record.

Q Sure. We looked at it before, I think it's Exhibit 1053.

Do you have it, sir?

A Yes.

Q Okay. And you would agree that prior to JHU even applying for the patent at issue in this case, BMS had publicly posted this study record explaining that the purpose of the study is to examine whether nivolumab alone or in combination with ipilimumab would demonstrate a meaningful objective response rate in patients with recurrent and

metastatic colon cancer who also have a specific biomarker in their tumors, right?
A That's correct.
Q Was that specific biomarker that BMS was referring to MSI positive?
A MSI positivity, yes.
Q And you would agree that as of February 10, 2014, BMS considered their study number NC202060188 worth performing, right?
A Correct.
Q And you would agree that as of the critical date in this case, BMS considered their study number NCT2060188 worth performing, right?
A Yes. And we actually performed many clinical trials that failed. So considered worth performing was not an indication of successful outcome.
I wish it was.
Q Now, the study that we've been referring to No. NCT02060188, this is the study involving nivolumab and MSI-High colorectal

cancer patients, right.?
A MSI-High colorectal cancer patients are included in the study, yes.
Q Do you recall using the phrasing in your declaration --
Let me try this again.
Do you recall using the phrasing in your October 4, 2024, declaration, "worth performing" as it relates to a clinical study.
A Can you point me to the language?
Q Well, I'm just asking, sitting here today, without looking at your declaration, do you have any recollection whatsoever if you ever used the phrase "worth performing" in the context of a clinical study?
A I've used that phrase many times in my life, I don't remember if that is a phrase that I used in this particular declaration.
Q Okay. So looking at your October 4, 2024, declaration you can turn your attention to Paragraph 186.

Let me know when you have it.
A I have it.
Q And you see in the first sentence of your declaration you testified "Prior to the actual release of JHU's trial results there was substantial skepticism from experts that such a study was worth performing."
Do you see that?
A That's true.
Q And the study that you're talking about is a study that was disclosed in the posted MSI study record, right?
A That's true.
Q When you say the actual release of the JHU's study results, what data are you talking about there?
A The publication in the New England Journal paper.
Q You're talking about May 30th, 2015?
A Is that when it was published, I don't remember.
Q Okay. Well, you would agree with me

that as of the February 2014, publication date of the study record for the BMS NCT2060188 study involving nivolumab, BMS considered that study worth performing, right?

A I agree.

Q Now, you're not taking the position in this case that BMS passed up an opportunity to study pembrolizumab in MSI-High colorectal cancer patients, right?

A BMS was not in a position to or would not would have wanted to study pembrolizumab. BMS would have wanted to study nivolumab.

Q I just want to be clear. So you are not taking the position, in this case, that BMS passed up an opportunity to study pembrolizumab in MSI-High colorectal cancer patients, right?

A Correct.

Q And you do agree that prior to the critical date in this case, BMS did take the opportunity to sponsor a study involving an

anti-PD-1 therapy in MSI-High colorectal cancer patients, right?
A Correct.
Q And you do agree that BMS took the opportunity before the critical date in this case --
A Correct.
Q Okay. I didn't finish my question. Let me try it again.
You do agree that BMS took the opportunity before the critical date in this case to do a study similar to the study disclosed in MSI-High study record, right?
MR. MILLER: Objection. Form.
A It is testing I believe one of the same hypotheses that would be tested in the JHU trial.
Q Okay. You testified in your declaration October 4, 2024, declaration that when JHU's trial results were publicized, there was a strong sense within BMS that we had missed out on a tremendous opportunity, do you

recall that?
A I recall that was the feeling within BMS at the time.
Q Okay. And at the time as you testified in your declaration, you're referring to when the JHU trial results were publicized, right?
A Yes.
Q And by this time BMS, had already undertaken a study involving their anti-PD-1 drug nivolumab in MSI-High colorectal cancer patients, right?
A Yes. But it was lagging behind the JHU trial. So the regret was we didn't jump on earlier when we had an opportunity back in, I believe 2013, to partner with Johns Hopkins. We turned it down then.
Q Okay. But you do appreciate that the posting of the BMS study involving the nivolumab in MSI-High colorectal cancer patients was posted publicly before JHU even applied for the patent at issue, in this case, right?

A I believe that's correct.
Q So would you agree with me that -- let me ask it this way.
Would you agree that by the critical date in this case JHU had initiated it's own work to conduct a clinical trial in MSI-High patients involving an anti-PD-1 therapy?
A I believe the answer to your question is yes, but I want to make sure I understand your question correctly, so could you repeat it.
Q Do you appreciate -- yeah, let me make sure my question --
Do you appreciate that by the critical date, in this case, BMS had initiated its own work to conduct a clinical trial in MSI-High patients involving an anti-PD-1 therapy?
A Yes.
Q And would you agree that BMS took the opportunity to perform a study of an anti-PD-1 therapy in MSI-High colorectal cancer patients prior to the actual release

of the trial results from the study disclosed in the MSI-High study record that we've been discussing today?

A Yes. Bristol Myers changed their mind about the value of conducting such a trial. That doesn't mean that they were certain of the outcome, but they changed their mind about the value and I think once the data came out from Johns Hopkins they regretted having made that initial decision not to partner with Johns Hopkins.

Q Now, this trial involving nivolumab NCT2060188, you refer to that trial in your October 4, 2024, declaration as a contemporary trial to the trial identified in the study record, right?

A They overlapped.

Q I didn't ask if they overlapped. My questions different.

The BMS study involving nivolumab with the number NCT2060188, is a trial that you refer to in your sworn declaration as a

contemporary trial to the trial identified in the study record we've been discussing today, right?

A Yes. And I said that they overlap, I think that's a similar meaning.

MR. MILLER: Preston, we've been going well over an hour, is this a good break time.

MR. RATLIFF: Would you like to take a break, Dr. Lonberg?

THE WITNESS: Yes. Please.

MR. RATLIFF: Okay. Let's take a break.

(Whereupon, a recess was taken from 5:56 PM until 6:09 PM.)

BY MR. RATLIFF:

Q Doctor, can you look at the study record for the BMS nivolumab study, this is Exhibit 1053.

A Okay, yes.

Q And actually before we do that, at any point in time today during the breaks did you

discuss your deposition testimony?
A I made an offhand hallway comment about the style of the deposition.
Q Okay. And at any point in time during any of the breaks today, did you discuss this case?
A No.
Q So let's take a look at the study record, this is Exhibit 1053.
And you would you agree that the POSA would have seen posted the official title of this study, right?
A Yes.
Q And the official title of the study of nivolumab, and nivolumab plus ipilimumab in recurrent metastatic colon cancer; is that right?
A The official title is a Phase II clinical trial of nivolumab and nivolumab plus ipilimumab in recurrent and metastatic microsatellite-High, MSI-H colon cancer.
Q Thank you. And when you reviewed the

'393 Patent at Page 2, that refers to this version of the study record, right?
A Are you talking about references.
Q I'm talking about if you go to the '393 Patent.
A Yes.
Q And you looked at Page 2, right?
A And by Page 2 you --
Q The second page of the patent.
A Right. It's just the patent starts out with references cited and then it goes into figures, are you talking about that as the page number or are you talking about the beginning of Column 1 and Column 2.
Q Right. So I'm talking about the section that says references cited on Page 2, so not the column to the patent, but where it actually says Page two.
A Yes.
Q Okay. And you see there's a section entitled other publications?
A Yes.

Q Do you see on Page 2 it refers to the version one of the study record for the BMS nivolumab trial, right?
A There is -- every version seems to be cited include, walk my way down, I don't see version one, can you point out where it is, I see version 32, version 33, version 34.
Q If you turn your attention to where it reads other publications.
A Yes.
Q Do you see that? And do you see where there's indicated study record versions of the study record that we've been discussing that's at issue in this case?
A Yes.
Q And that's NCT01876511, you see that right?
A Right. And I see multiple versions cited including versions nine, eight, seven, six, five, four, 38, 37, 36, 35, 34, 33, 32, but I don't version one, yet.
Q Okay. So what I'm asking about is the

BMS trial involving nivolumab, the clinical trial identifier NCT2060188?
A Yes.
Q If you go towards the middle of the page on the left-hand side, do you see the first entry that references NCT2060188?
A The first reference to NCT2060188 is the very first publication and that's version 32.
Q Let's make sure we're looking at the same thing.
You have Page 2 of the '393 Patent, right?
A Yes.
Q No worries.
A Yes, I found it, version one, yes.
Q So you see on Page 2 of the '393 Patent, a reference to version one of the BMS trial involving nivolumab and MSI-High colorectal cancer patients, right?
A Yes.
Q And would you agree with me that prior to the critical date in this case, the person

of ordinary skill would have been aware of both the BMS clinical trial involving an anti-PD-1 inhibitor and MSI colorectal cancer patients, as well as the trial that's disclosed in the study record, Exhibit 1005?

A Yes.

Q So you would agree with me that prior to the critical date in this case, the POSA would have been aware of at least two clinical trials testing an anti-PD-1 inhibitor in MSI-High colorectal cancers, right?

A Correct.

Q And the publication of the BMS study record came about nine months before JHU even filed it's first professional application relating to the '393 Patent, right?

A Yes.

Q And that publication of the BMS study record came more than 17 months before the critical date in this case, right?

A Yes.

Q And you would agree that prior to the critical date in this case, the POSA would have knowledge of 31 updates to BMS study records about testing nivolumab in MSI-High colorectal cancer patients, right?
A At least.
Q A least 31, right?
A Yes.
Q Now, you say in your declaration that prior to the actual release of JHU trial results, there was substantial skepticism from experts that "such a study was worth performing," right?
A That's correct.
Q And when the study record, and this is Exhibit 1005, was published on June 10, 2013, did you write to JHU expressing skepticism that the study was worth performing?
A No. In fact, I had already expressed enthusiasm to Drew Pardoll about doing such a clinical trial.
Q Right. So when the study record was

posted on clinicaltrial.gov you also didn't write to anyone at the FDA expressing skepticism that the study was worth performing, right?

A No.

Q And when the study record was published on clinicaltrials.gov you also didn't write to anyone at Merck expressing skepticism that the study was worth performing, right?

A No. Of course not.

Q And when the study record was published on clinicaltrials.gov, you didn't write to anyone at all expressing skepticism that the study was worth performing, right?

A No.

Q Are aware of anyone ever writing to JHU expressing skepticism that the study disclosed in the study record was not worth performing?

A No.

Q Are you aware of anyone ever writing to the FDA that the study disclosed in the study

record was not worth performing?
A No.
Q Are you aware of anyone ever writing to the NIH that the study disclosed in the study record was not worth performing?
A No.
Q Are you aware of anyone ever writing to clinicaltrials.gov, stating that the study record was not -- let me try that again.
Are you aware of anyone ever writing to clinicaltrials.gov, that the study records disclosed -- I'm sorry, let me try this again.
Are you aware of anyone ever writing to clinicaltrials.gov, that the trial disclosed in the study record was not worth performing?
A No.
Q Are you aware of anyone ever calling the FDA, clinicaltrials.gov, the NIH, or anyone to state that the trial that's disclosed in the study record was not worth performing?
A No.

Q Do you know if in the month after the trial results were released and before the critical date in this case, if there was anyone who expressed skepticism that the trial disclosed in the posted study record was not worth performing?
A No. I don't recall. I never heard a phrasing like that, that a trial was not worth performing.
Q Now, in this case you're not taking the position that as of the posting of the study records, Exhibit 1005, Merck was skeptical of the study.
You're not taking that position, right?
A I don't have any internal knowledge of what was going on at Merck. The only thing I know is that Merck declined funding the trial.
Q And when you say that you're aware that Merck declined funding the trial, from where did you get that information?
A From Drew Pardoll.

Q And Drew Pardoll -- excuse me?
A That's my memory.
Q That's your memory.
And Drew Pardoll is one of the named inventors on the '393 Patent, right?
A Yes.
Q And is it fair to say that Drew Pardoll has an interest in the outcome of this case?
A Yes.
Q Now, you understand that at the time that the study record was posted, Exhibit 1005, that Merck was a collaborator for that study, right?
MR. MILLER: Objection. Form.
A I don't know that that would be clear from the study record. I know now that they provided a drug for free. They provided pembrolizumab.
Q It's your understanding that Merck provided drug for free to John Hopkins to conduct the study that's disclosed in the study record?

A That's standard practice. Many drug companies have programs like that, and Merck has -- they still have an active program where they will provide pembrolizumab for free for clinical studies. Obviously, they have restrictions on how you share the data, but they provide the drug. That's quite common.

Q Okay. I'm not asking anything about standard practice. I'm asking specifically about Merck.

A Yeah, well, this is about Merck. I'm on the board of a company right now where we've gotten study drug from Merck. We've gotten pembrolizumab from Merck.

Q Okay. And so here's my question: Is it your understanding that Merck provided pembrolizumab for free to John Hopkins as part of conducting the clinical trial that's described in the study record, Exhibit 1005?

A That is my current understanding, but I don't know when I came to that understanding.

Q Okay. And the study record, did you review that carefully?
A The study record, yes.
Q Yes.
Did you?
A Yes.
Q Okay. And do you recall whether or not the study record indicated that Merck was a collaborator for the study?
A Well, let me go look at it. What's the number again?
Q Well, I was asking -- I was asking you, sitting here today, do you have any recollection one way or not if Merck was indicated as the collaborator in that study record?
A Yes. They're indicated as a collaborator.
Q Okay. And as a collaborator, you understand that Merck had provided support to conduct the clinical study that's described in the study record, right?

MR. MILLER: Objection. Form. Scope.
A I don't -- I wouldn't have known what the level of collaboration would be in this -- from the study record. It could have been everything from supplying drug to analyzing biopsies. There's a number of different ways that drug companies collaborate with institutional investigators.
Q Right. And for the study that's described in the study record that we've been discussing, sitting here today, you don't have any knowledge of the extent of the support that Merck provided, right?
A I have some knowledge in that they provided drug.
Q But beyond that, do you have any additional knowledge as to what support Merck provided as part of that study?
A Not that I can recall.
Q You have a copy of the '393 Patent, right, sir?
A Yes.

Q And can you turn your attention to the claims of the '393 Patent.
A Yes.
Q And looking at Claim 1, would you agree that all that Claim 1 requires in terms of success is treating a colorectal cancer patient, right?
A With mismatch repair deficient -- deficiency, or --
Q Okay. Let me try that again.
So you would agree that in terms of success, all that Claim 1 of the '393 Patent requires is treating a MSI-High colorectal cancer patient with pembrolizumab, right?
A Right. But you wouldn't be able to treat an MSI-High or dMMR deficient patient unless you had first identified that patient by testing and then, in response to the outcome of that test, treating.
Q And in your opinion, is there any requirement set forth in Claim 1 of the '393 Patent as to how well the colorectal

cancer patient has been treated?
MR. MILLER: Objection. Form.
A It says "therapeutically effective."
Q Well, it says you have to give a therapeutically effective amount of pembrolizumab, right?
A Right.
Q But do you have any opinion with respect to Claim 1 if there's any level of treatment required to the MSI-High colorectal cancer patient beyond simply treating the patient?
MR. MILLER: Objection. Form.
A I don't understand what you mean by "any level of treatment."
Q Do you have any opinion as to the extent of treatment that's required by Claim 1 of the '393 Patent to a colorectal cancer patient?
MR. MILLER: Objection. Form.
A You mean the -- the length of time that the patient is treated?
Q I mean the outcome that would happen --

A Oh.
Q -- for the cancer patient?
A I see.
MR. MILLER: Let me just -- objection.
Form.
A I completely misunderstood your question. I apologize.
Q No worries.
A So what you're asking -- now rephrase your question again now that I understand what you meant by the level.
Q Right. So looking at Claim 1, do you have any opinion as to the -- if Claim 1 has a required outcome for the treatment that's called for by Claim 1?
MR. MILLER: Objection. Form.
A All I can say is that it is implied because the patient is treated with a therapeutically effective amount of pembrolizumab.
Q An effective to accomplish what?
A Patient benefit.

Q So in your belief with respect to Claim 1, all that's required in terms of the outcome is a patient benefit; is that fair?
A Yes. The patient's benefit from the therapy.
Q And do you share that same belief with respect to Claim 14? All that's required is a benefit to the patient?
A Patient 14 (sic) cites a particular subset of patient benefit, and that is progression, reducing the risk of cancer progression.
Q Okay. And you're talking about Claim 14, right?
A Yes.
MR. RATLIFF: Okay. Doctor, I may be able to finish up my questioning if we take a break. Although if your counsel has questions for you, then I have another opportunity to ask you more questions.
So let's take about a ten-minute

break, and let me see what I can do.

THE WITNESS: Okay.

(Whereupon, a recess was taken from 6:32 PM until 6:45 PM.)

Q Doctor, during the break did you discuss any of your testimony today?

A No.

Q And, Doctor, during the break did you discuss this case at all?

A No.

Q Doctor, would you agree that the BMS MSI-High nivolumab trial that you refer to as a contemporary trial of the trial disclosed in the MSI-High study record was not a failed trial?

A I don't remember the outcome of the trial. I don't remember the data.

Q Sitting here today, you don't --

A I don't recall the data, no.

Q And so just to be clear, do you recall whether or not the trial was considered a success, the BMS MSI-High nivolumab trial?

A I don't remember what the outcome was.
Q Okay. And do you know one way or not whether the FDA granted nivolumab accelerated approval for MSI-High colorectal cancer based on the NCT2060188 BMS study?
A No. I don't recall.
Q Okay. You don't have a recollection.
So since you don't have a recollection maybe we can take a look at a new exhibit, and it's Exhibit No. 1120.
MR. RATLIFF: This is a new exhibit that we're introducing.
(Whereupon, "FDA grants nivolumab accelerated approval for MSI-H or dMMR colorectal cancer" was marked as Exhibit 1120 for identification as of this date.)
Q And similar to the others, let me know when you have it, Doctor.
TECH WELCH: 1120 is uploading.
MR. MILLER: Keli, can you tell if

it's uploaded?

TECH WELCH: I will double-check.

MR. MILLER: I'm not seeing it yet.

Q And you have the new exhibit, 1120, Doctor?

A Yes, I do.

Q And you testified earlier that just sitting at that time when I asked you the question, you had no recollection of whether or not the BMS MSI-High colorectal cancer trial that we have been discussing, NCT2060188, was a success or failure; is that right?

A That's correct.

Q Okay. And I've placed in front of you new Exhibit 1120, which is a press release taken from the FDA's website that I can represent to you entitled "FDA grants nivolumab accelerated approval for MSI-High or dMMR colorectal cancer."

A Yes. I remember this very well.

Q Okay. And you were working at BMS at

the time that this press release was issued, right?
A Yes. That's correct.
Q And does this refresh your recollection as to whether or not the BMS MSI-High colorectal cancer trial involving nivolumab was a success or failure?
A Yes. Because it links the 02060188 to CHECKMATE 142, and I just didn't have a memory of that linkage or not.
Q Okay. And so sitting here today now, do you have an understanding of whether or not that trial was successful or was a failed trial?
A Yes. It was a success.
MR. RATLIFF: Now, Doctor, I don't have any additional questions for you at this time. Your counsel may have questions. And again, as I mentioned, depending on your counsel's questions, I may have additional questions for you and additional time with you.

MR. MILLER: You're passing the witness?
MR. RATLIFF: I am.
MR. MILLER: Thank you.
Doctor, I'm going to try to do this without moving us all around.

EXAMINATION BY
MR. MILLER:

Q The rules are the same. Pause after my question to allow counsel to interpose his objection. While this isn't videotaped, may as well keep looking at your screen as you've been doing all day today.
Is that all right?
A Yes.
Q All right. Counsel asked you this, but during the break did we review any of the questions that I was going to pose to you on redirect?
A No.
Q Did we talk at all about the questions that I might pose?

A No.
Q All right. You were asked at the beginning of the day a number of questions regarding whether you're an oncologist, right?
A Yes.
Q And you are not?
A No.
Q And you're not a medical doctor?
A No.
Q Could you then explain what it is in your background and experience that qualifies you as a person of ordinary skill in the art in the technology of the '393 Patent as of its critical date?
A I have been --
MR. RATLIFF: Objection. Beyond the scope.
A I have been conducting research in cancer immunotherapy for almost three decades. I -- the very first checkpoint blockade therapy that is now

approved to go into the clinic was ipilimumab. That came out of my lab.

The second checkpoint blockade target was PD-1. The very first PD-1-targeted drug to go into the clinic that is now approved is nivolumab. That also came out of my lab.

The third target -- checkpoint target that has lead to a -- an approved therapy is LAG-3, and that approved antibody is relatlimab, which is a dosing combination with nivolumab, and that came out of my lab.

There are now two combination therapies, combination checkpoint blockade therapies that are approved, ipilimumab plus nivolumab and relatlimab plus nivolumab. And both of those combinations came out of my lab.

I spent a decade at Bristol Myers Squibb. I was biology head of oncology drug discovery. And for a period of time all early stage cancer clinical trials reported to me, and that included a number of physicians. And I don't think a Fortune 500

company would have trusted me to run clinical trials and have physicians reporting to me if they didn't consider me to be at least a person of ordinary skill in the art.

Q In 2015, to your knowledge, was pembrolizumab approved for doctors to prescribe to their MSI-High CRC patients?

A No.

Q Does that fact influence your understanding of what the technical training and/or experience of a person of skill in the art would have had as of July 2015 in the context of the '393 Patent?

A Yes.

MR. RATLIFF: Objection. Beyond the scope.

Q How so?

A I think that --

MR. RATLIFF: Objection. Beyond the scope.

Q You can answer.

A I think that, given that this was still

an experimental therapy and a non-tested hypothesis, that the important criteria for determining one who is as -- has ordinary skill in the art is going to lean heavily toward experience with an understanding of the basic science, immunology, oncology and an understanding of immunotherapy and an understanding of clinical trial design.

Q Thank you.

You were also asked by counsel for Merck a number of questions about the study record from 2013, the Hopkins study record, which is Exhibit 1005.

Do you recall generally receiving those sorts of questions?

A Yes.

MR. RATLIFF: Objection. Form.

Q I'll start with the time frame of June 2013.

As of June 2013, would a person of ordinary skill in the art in the field of the '393 Patent have recognized MSI-High as a

biomarker or -- yeah, biomarker in colorectal cancer patients for responsiveness to pembrolizumab?

A No.

Q Before Dr. Le presented her results at the ASCO conference in May of 2015, would a person of skill in the art in the field of the '393 Patent have recognized MSI-High as a biomarker for responsiveness to pembrolizumab in MSI-High colorectal cancer patients?

A No.

MR. RATLIFF: Objection. Beyond the scope.

Q Before the contemporaneous -- before the publication of the New England Journal article, also in May of 2015, and in fact on the same day as the ASCO presentation by Dr. Le; would a person of ordinary skill in the art in the field of the '393 Patent have recognized MSI-High as a biomarker for responsiveness to pembrolizumab in MSI-High colorectal cancer patients?

MR. RATLIFF: Objection. Beyond the scope.

A No.

Q You were asked by counsel for Merck a number of questions about the claims of the '393 Patent, and I have some very short questions about that.

If you could take that out and turn your attention to Claims 1 and 14.

A Yes.

Q Now, you were asked the contents of Claim 1 whether there were two steps to that claim.

Do you recall that?

A Yes. I recall that.

MR. RATLIFF: Objection. Leading.

Q Does the claim itself explain what those two steps are intended to achieve?

MR. RATLIFF: Objection. Form.

A Yes.

Q What is that?

MR. RATLIFF: Objection. Form.

A The purpose of the first step is determining that the patients colorectal cancer is a Microsatellite Instability-High or mismatch repair deficient; and the purpose of the second step, which is a response to that determination is to treat the patient with a therapeutically effective amount of pembrolizumab.

Q What do the first three lines of the claim tell you as a -- looking through the lens of a person of skill in the art?

A It's teaching a person of skill in the art that this is a novel, useful method for treating a subset of colorectal cancer patients.

Q Turning your attention to Claim 14.

Same basic question. The first here, the first four lines of the claim. What would those teach a person of skill in the art about the purpose of the ensuing two steps?

MR. RATLIFF: Objection. Beyond the

scope.
A That the purpose is to reduce the risk of cancer progression or increase overall survival in a human patient.
Q Thank you. You were asked about a number of references today, in particular, I believe it was in the context of your discussion of the Champiat reference, you were trying to explain the difference between tumor mutational load and mutational heterogeneity, and I think you got you cut off in parts of that explanation. Could you provide that explanation to us?
MR. RATLIFF: Objection. Leading.
Objection. Form.
A Well, the hypothesis that Champiat and Soria and the other authors were putting forth was a hypothesis that was a potential explanation for the discordance between two mutational burdens and responses that illustrated by the sensitivity of renal cell cancer to checkpoint blockade, PD-1 blockade

compared to other tumors such as DLBCL, ovarian, GBM, that have higher tumor mutational burden than RCC, but are not sensitive to PD-1 blockade. That hypothesis, it's an interesting hypothesis. That hypothesis is, in fact, what is required for effective immunotherapy is the elicitation of a diverse immune response.

And I think that, well, it was an interesting hypothesis at the time, but there was also evidence already at the time that the diverse response was not, in fact, required and I would have started with the preclinical data from Bob Schreiber's lab showing that in a mouse tumor model that there might be one or two dominant antigens that are, in fact, entirely responsible for the immune destruction of tumors. Because deletion of those antigens resulted in tumors that grew out. And then that, I think was translated into the clinic for the work of Toni Ribas and colleagues from UCLA, where

they followed the diversification of immune response in patients that are treated with either CTLA-4 blockade or PD-1 blockade. And while they did see an expanding diversity of immune response in CTLA-4 blockade treated patients, they did not see that in the PD-1 treated patients.

Q Thank you. I'm going to switch gears a bit.

You were asked about Exhibit 1053, which was a Bristol Myers Squibb clinical trial posting, do you recall those questions generally?

A Yes.

Q Now, that clinical trial posting Exhibit 1053, is it your recollection that that was posted in 2014?

A That's my recollection, yes.

Q When was the JHU clinical trial posting done, and that's Exhibit 1005? Just what year if you recall.

A My recollection is 2013, but I don't

have that in front of me.

MR. RATLIFF: If you're going to help him with that, objection. Leading.

MR. MILLER: I am helping him with it exactly as I helped him with it throughout your entire deposition. I'm putting up the document for him to see.

A Yes. June 2013, that's -- my recollection was correct.

Q Which came first, the Bristol Myers or the Hopkins clinical trial posting?

A The Hopkins.

Q Did the Bristol Myers posting come after Dr. Pardoll sought support from Bristol Myers for its clinical trial?

MR. RATLIFF: Objection. Beyond the scope.

A My recollection is the conversations between Hopkins and Bristol Myers began in 2012, so a year earlier.

Q Did the posting of the JHU clinical

trial on clinicaltrials.gov have any influence on BMS's decision to pursue it's own clinical trial?

MR. RATLIFF: Objection. Leading.

A I don't remember it ever being discussed.

Q Did Bristol Myers Squibb publish any results from the clinical trial, Exhibit 1053 before the clinical date -- sorry, before the critical date of the '393 patent?

MR. RATLIFF: Objection. Beyond the scope.

A No.

Q Would a person of ordinary skill in the art have known the results of the Bristol Meyers clinical trial before the '393 Patent's clinical date?

A No. No.

Q You were shown at the very end of counsel's examination Exhibit 1120. Which was a press release where the FDA granted accelerated approval for MSI-High indication,

do you recall that?
A Yes. That was in 2017.
Q I was going to ask you what year it was, what year was that in?
A 2017.
Q It's fair to say that press release, Exhibit 1120, post dates the critical date by two years or thereabouts?
A Thereabouts.
Q The -- returning to the '393 Patent, you were asked about the citation on the second page?
A Yes and I think now I will have an easier time finding the second page. I apologize these pages are unnumbered -- oh, they are numbered now I see.
Q If I turn your attention to Pages 2 and 3.
A Okay.
Q Do you see citations to the Bristol Myers clinical trial NCT2060188, which begin mid way in the first column on Page 2?

A Yes.
Q And go to the end of that first column.
A Yes.
MR. RATLIFF: Objection. Leading.
Q And do the citations to the various versions of clinical trial encompass the entirety of the right hand column of Page 2?
A Yes.
Q And do the citations to the clinical trial encompass about three-fourths of the left column of Page 3 of the '393 Patent?
A That appears to be relatively accurate.
Q I believe you testified that in your account there were at least 31 citations to the various versions of that clinical trial?
A At least.
Q Does that strike you as John Hopkins trying to keep the Bristol Myers clinical trial a secret from the patent office during the prosecution of the '393 Patent clinical patent?
A No.

Q Do you have any understanding as to who funded the JHU clinical trial, the Phase II clinical trial, that emerged from Exhibit 1005?

MR. RATLIFF: Objection. Beyond the scope.

A Because my memory I can't place where I formed that opinion from, so I would have to say I don't recall.

Q Fair enough.

Do you recall whether Dr. Pardoll told you where Hopkins would get funding for to conduct that clinical trial, the Phase II clinical trial, that ensued from Exhibit 1005?

A I don't recall a conversation --

MR. RATLIFF: Objection. Beyond the scope.

Q Do you recall when Dr. Pardoll told you that Merck did not fund the Phase II clinical trial that ensued from Exhibit 1005?

MR. RATLIFF: Objection. Leading.

Objection. Beyond the scope.
A I don't have a recollection of the time.
Q Approximately?
MR. RATLIFF: Objection. Leading.
Objection. Beyond the scope.
A No.
Q Do you recall whether it was when you were still employed at Bristol Myers?
A Yes.
MR. RATLIFF: Objection. Form.
Q And so while you were employed at Bristol Myers, do you recall Dr. Pardoll telling you that Merck did not fund its clinical trial that ensued from Exhibit 1005?
A Yes.
MR. MILLER: Objection. Leading.
Objection. Beyond the scope.
Q When did you stop working at Bristol Myers Squibb?
A May 2019.
Q That's the hardest question of the day.
MR. MILLER: Thank you. That's all

the questions I have at this moment.
Pass the witness.
MR. RATLIFF: Let's take a break.
(Whereupon, a recess was taken from 7:13 PM until 7:22 PM.)
MR. RATLIFF: Okay. Doctor, I have no further questions for you at this particular time. Thank you for your time. I believe I'll be seeing you again with respect to some other cases, but thank you, and I'd like to also thank the court reporter and the remote tech for their services today.
MR. MILLER: Yes, thank you all. Thanks, Preston. Good to meet you.
COURT REPORTER: Do you want a copy of the transcript?
MR. MILLER: Just the transcript.
(Whereupon, this examination was concluded at 7:23 PM.)

_____

NILS LONBERG

Subscribed and sworn to
before me on this ____ day
of _____, _____.

_____
Notary Public

I N D E X

WITNESS: NILS LONBERG

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E X H I B I T S

EXHIBITS	DESCRIPTION	PAGE
Exhibit 2072	Declaration of Dr. Nils Lonberg, dated 10-4-24	9
Exhibit 1001	US Patent No. 11,591,393 B2, dated 2-28-23	22
Exhibit 1005	Study NCT01876511, dated 6-10-13	90
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Exhibit 1007	"Clinical Relevance of Microsatellite Instability in Colorectal Cancer," published 7-10-10	145
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C E R T I F I C A T E

I, KIARA MILLER,
a Shorthand Reporter and Notary Public of the State of New York, do hereby certify:

That the witness whose examination is hereinbefore set forth, was duly sworn or affirmed by me, and the foregoing transcript is a true record of the testimony given by such witness.

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.

Kiara Miller

KIARA MILLER