1 UNITED STATES PATENT AND TRADEMARK OFFICE
2 BEFORE THE PATENT TRIAL AND APPEAL BOARD
3 ----------X
4 MERCK SHARP & DOHME, LLC,
5 Petitioner,
6 CASE.: IPR2024-00240
7 -against-
8
9 THE JOHN HOPKINS UNIVERSITY,
10 Patent Owner.
11 ----------X
12
13 REMOTE DEPOSITION OF
14 NILS LONBERG, PH.D.
15 NEW YORK, NEW YORK
16 DECEMBER 20, 2024
17
18
19
20 REPORTED BY: KIARA MILLER
21 FILE NO.: 562907
22

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12
13 Deposition of NILS LONBERG, PH.D., taken on
14 behalf of PETITIONER, at REMOTE LOCATION, New
15 York, New York, commencing at 12:08 PM,
16 DECEMBER 20, 2024, before Kiara Miller.
17
18
19
20
21
22

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16

17 ALSO PRESENT:

18 ZOOM TECH, KELI WELCH

19 MATT PEARSON, ESQ., AKIN GUMP STRAUSS HAUER & FELD

20 NATHAN HELPER, PAUL HASTINGS

21 JINNY LIM, PAUL HASTINGS

22 KAREN MOREIRA, IN-HOUSE COUNSEL, MERCK

1 N I L S L O N B E R G, after having first been duly
2 sworn by a Notary Public of the State of New York,
3 was examined and testified as follows:
4 COURT REPORTER: Please state your
5 name and address for the record.
6 THE WITNESS: Nils Lonberg, 168 Bardet
7 Road, Woodside, California 94062.
8 MR. RATLIFF: Good morning. My name
9 is Preston Ratliff. I'm with the Paul
10 Hastings law firm on behalf of the
11 petitioner Merck. And I'm joined
12 today by other Paul Hastings' members
13 representing Merck.
14 Jessica Stauring, Jinny Lim, Nathan
15 Helper, Rachel Wu Hankinson. In
16 addition to that, Ms. Karen Moreira,
17 in-house counsel for Merck is joining
18 us, as well as Mr. Mark Stewart.
19 EXAMINATION BY
20 MR. RATLIFF:
21 Q Good morning, Doctor. Will you please
22 state your full name for the record.

1 A Nils Lonberg.
2 Q Please state your residence address.
3 A 168 Bardett Road, in Woodside,
4 California 94062.
5 Q How are you feeling today?
6 A Good.
7 Q You understand that you're testifying
8 under oath today, right?
9 A Yes.
10 Q Is there any reason you cannot testify
11 truthfully today?
12 A No.
13 Q Now, you're an executive at a venture
14 capital firm, right?
15 A I am an executive and resident.
16 Q Okay. So you're an executive and
17 resident at a venture capital firm, right?
18 A I'm half time there, yes.
19 Q You are not an oncologist, correct?
20 A No.
21 Q You've never been an oncologist,
22 correct?

1 A Correct.
2 Q You're not a medical doctor, correct?
3 A Correct.
4 Q You have never been a medical doctor,
5 right?
6 A Correct.
7 Q A colorectal cancer patient has never
8 been under your medical care, right?
9 A Correct.
10 Q A cancer patient has never been under
11 your medical care, right?
12 A Correct.
13 Q You have never prescribed pembrolizumab
14 to a cancer patient, right?
15 A Correct.
16 Q You have never prescribed any anti-PD1
17 drug to a cancer patient, right?
18 A Correct.
19 Q You have never prescribed any anti-PD1
20 or anti-PDL1 therapy to a cancer patient,
21 right?
22 A Correct.

1 Q You have never prescribed any
2 pharmaceutical compound to any cancer
3 patient, right?
4 A Correct.
5 Q Doctor, do you have any documents with
6 you, whether in hard copy or loaded on a
7 computer?
8 A I have my declaration of October
9 4th, 2024 and I have my declaration of
10 March 14th, 2024, and I have a copy of the
11 '393 Patent.
12 Q Okay. And are there any markings on
13 those documents that you have with you?
14 A There are no markings.
15 Q Any pads, post-it notes, or any
16 highlighting of any kind?
17 A No.
18 Q Now, Doctor, you read the '393 Patent
19 that is at issue in this case, right?
20 A Correct.
21 Q You read the entire patent, right?
22 A Correct.

1 Q When you read the '393 Patent, you
2 understood it, correct?
3 A Correct.
4 Q You were not confused by any of the '393
5 Patent's contents, right?
6 A I was not confused.
7 Q And when you read the '393 Patent, the
8 statements in the patent read to you as being
9 truthful, right?
10 A Correct.
11 Q And when you read the patent, the
12 statements and data in the '393 Patent read
13 to you as being accurate in terms of the
14 science, right?
15 MR. RATLIFF: Objection, form.
16 A Could you repeat the question.
17 Q Sure. When you read the '393 Patent,
18 the statements and data in that patent read
19 to you as being accurate in terms of the
20 science, right?
21 A Correct.
22 Q You reviewed the file history of the

1 '393 Patent, right?
2 A I don't recall if I reviewed the file
3 history.
4 Q Sitting here today, you don't recall if
5 you reviewed the file history?
6 A I don't recall if documents I reviewed
7 were the file history.
8 Q Okay. Let me refresh your recollection.
9 (Whereupon, Declaration of Dr.
10 Nils Lonberg, dated 10-4-24 was
11 marked as Exhibit 2072 for
12 identification as of this date.)
13 Q You have your declaration with you,
14 right?
15 A Yes.
16 Q And this is the October 4, 2024
17 declaration that you have?
18 A Yes.
19 Q And if you can turn to Paragraph 7 of
20 this declaration.
21 Let me know when you have it, sir.
22 A I've got it. Yes.

1 Q Do you see that you say in Paragraph 7
2 that you reviewed the '393 Patent and it's
3 accompanying prosecution history?
4 A Yes.
5 Q Does that refresh your recollection that
6 you reviewed the file history for the '393
7 Patent?
8 A Yes. Example 1002 must have been the
9 document you're referring to. Which you
10 called file --
11 Q And you read the entire file history,
12 right?
13 A That -- I don't recall if I read
14 everything.
15 Q So you're not sure if you read
16 everything in the file history?
17 A I don't know. I reviewed documents that
18 were given to me, document 1002, but I don't
19 know if that is the entire file history.
20 Q Okay. Well, in the document that was
21 given to you, 1002, did you understand
22 everything within that document?

1 A Yes.
2 Q And you were not confused by anything
3 that you read in that document, Exhibit 1002,
4 right?
5 A Correct.
6 Q Now, in your analysis for this case, you
7 used July 10, 2015 as the critical date,
8 right?
9 A Correct.
10 Q And JHU's counsel informed you that the
11 critical date represents the earliest
12 possible priority date to which the claim of
13 the '393 Patent are entitled, right?
14 A I was --
15 Q Did you hear me, Doctor?
16 A I was told by the Hopkins' attorneys
17 that the July 10th date was the critical
18 date.
19 Q Right. And the Hopkins' attorneys
20 informed you that the critical date
21 represents the earliest possible priority
22 date to which the claims of the '393 Patent

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

1 critical date represents the earliest
2 priority date to which the claims of the '393
3 Patent are entitled, right?
4 A Yes. I think it -- I think the wording
5 in my declaration is, "The earliest possible
6 priority date to which the challenged claims
7 of the '393 Patent are entitled."
8 Q And do you understand that all of the
9 claims in the '393 Patent have been
10 challenged in this case?
11 A Where in my declaration do I say that?
12 Q I'm asking you. Do you understand that
13 each and every claim has been challenged in
14 this case?
15 A I'll take your word for it.
16 Q I'm asking you. If you don't
17 understand, you can just say "I don't
18 understand that."
19 Sitting here today, do you have an
20 understanding whether or not each and every
21 one of the claims of the '393 Patent have
22 been challenged in this case --

1 A I don't have an understanding --
2 Q -- yes or no?
3 A I don't have an understanding that there
4 are claims that were not challenged.
5 Q Okay. Now, and you understood that the
6 July 10, 2015 date represents the earliest
7 possible priority date to which the
8 challenged claims of the '393 Patent are
9 entitled, right?
10 A Correct.
11 Q Now, in your October 4, 2024
12 declaration, you used the phrasing, "At the
13 time of the invention of the '393 Patent."
14 Do you recall using that phrasing?
15 A Can you point me where in my
16 declaration?
17 Q Well, let me ask you first.
18 Do you recall at all using that
19 phrasing, "At the time of the invention of
20 the '393 Patent" in your declaration?
21 A I would like to see where in the
22 declaration you are referring to.

1 Q We'll go there. But sitting here right
2 now, do you recall using that phrasing at the
3 time of the invention of the '393 Patent, yes
4 or no?
5 A I would like to see where in the
6 declaration I state that.
7 Q So let me try my question one more time.
8 Sitting here right now, do you have any
9 recollection whether or not you wrote in your
10 declaration, the phrase, "At the time of the
11 invention of the '393 Patent"?
12 MR. MILLER: Objection. Asked and
13 answered.
14 A There's a hundred pages in this
15 declaration. I don't recall, sitting here
16 right now, every -- every phrasing.
17 Okay. And you appreciate I'm not asking
18 if you recall every phrasing. I'm asking you
19 about one specific phrase.
20 Do you recall, sitting here right now,
21 whether or not you used the phrasing, "At the
22 time of the invention of the '393 Patent" in

1 your declaration, yes or no?
2 MR. MILLER: Objection. Asked and
3 answered.
4 A I'd like to get this correct, which is
5 why I'd like to see where you're pointing to.
6 Q Sir, I just want to -- if you don't have
7 a recollection right now, you can just tell
8 me.
9 Do you recall right now whether or not
10 you used the phrasing, "At the time of the
11 invention of the '393 Patent" in your
12 October 4, 2024 declaration?
13 MR. MILLER: Objection. Asked and
14 answered.
15 A I don't have a recollection of the
16 entire -- all the words in the entire
17 declaration. And so rather than agree to a
18 particular phrasing that you described, I
19 would like to see where in the declaration
20 that is written.
21 Q Well, sir, do you appreciate I did not
22 ask you whether or not you had an entire

1 recollection of all of the words that you
2 used in your declaration? You appreciate
3 that, right?
4 A Correct.
5 Q You appreciate that that was not my
6 question -- okay, great.
7 So let's turn to your declaration, and
8 let's look at Paragraph 53. And in
9 particular, I'll turn your attention to
10 Heading F.
11 Let me know when you're there.
12 A Okay. I'm there.
13 Q And do you see in Heading F, you write:
14 State of the prior art "At the time of
15 the invention of the '393 Patent."
16 Do you see that?
17 A Are you referring to Paragraph 53?
18 Q I'm referring to the Heading F.
19 A Oh, the heading. Sorry. I apologize.
20 Q No worries.
21 A "State of the prior art at the time of
22 the invention of the '393 Patent," is what

1 Heading F says.
2 Q Right. So you wrote in Heading F:
3 State of the prior art "At the time of
4 the invention of the '393 Patent," right?
5 A Correct.
6 Q And for clarity, what date did you
7 consider to be "At the time of the invention
8 of the '393 Patent"?
9 A July 10, 2015.
10 Q Okay. So it's the same date as the
11 critical date, right?
12 A Correct.
13 Q Now, you understand that JHU filed a
14 provisional patent application on
15 November 13, 2014, right?
16 A Correct.
17 Q And you understand that JHU filed that
18 provisional patent application before the
19 time of the so-called invention date, right?
20 MR. MILLER: Objection, form.
21 A That was prior to the critical date of
22 July 10, 2015.

1 Q And it was also prior to what you call,
2 "At the time of the invention of the '393
3 Patent," right?
4 A Correct.
5 Q Did you ever ask anyone, as part of your
6 work in this case, why JHU filed a
7 provisional patent application on
8 November 13, 2014 before the time of its
9 so-called invention?
10 MR. MILLER: Objection, form.
11 A I don't recall any specific conversation
12 with the John Hopkins' attorneys.
13 Q I'm not asking if you recall any
14 specific conversation. My question is
15 different.
16 Did you ever ask anyone, as part of your
17 work in this case, why JHU filed a
18 provisional patent application on
19 November 13, 2014, before the time of it's
20 so-called invention?
21 MR. MILLER: Objection, form.
22 A I have only spoken about this case with

1 the John Hopkins attorneys, so it would have
2 been a conversation with the John Hopkins
3 attorney and I don't recall every specific
4 conversation.
5 Q And you realize I'm not asking you to
6 recall every specific conversation that you
7 had with the JHU attorney, right?
8 A Correct.
9 Q So my question is asking about something
10 very specific. Let me ask it again.
11 Did you ever ask anyone as part of your
12 work in this case, why JHU filed a
13 provisional patent application on
14 November 13, 2014, before the time of it's so
15 called invention?
16 MR. MILLER: Objection. Form.
17 A I don't recall a specific conversation.
18 Q Now, you read the background of
19 invention section of the '393 Patent, right?
20 A Yes. The specifications, I read the
21 entire specification.
22 Q You read the entire, okay.

1 Now, do you have any reason to believe
2 that what's described in the specifications
3 of the '393 Patent is not true?
4 A I have no reason to believe that.
5 Q Do you have any reason to believe that
6 what's described in the specification of the
7 '393 Patent is not accurate?
8 A No.
9 Q Did you have any reason to believe that
10 what is described in the specification of the
11 '393 Patent is not to be believed?
12 A No.
13 Q Do you have any to reason to believe
14 that what's described in the specification of
15 the '393 Patent does not reflect the belief
16 of the named JHU inventors at the time that
17 they applied for the '393 Patent?
18 MR. MILLER: Objection. Form.
19 A Could you repeat the question.
20 Q Sure.
21 Do you have any reason to believe that
22 what is written in the specification of the

1 '393 Patent, does not reflect the belief of
2 the named JHU inventor at the time that they
3 applied for the '393 Patent?
4 MR. MILLER: Same objection.
5 A No. I don't.
6 Q Now, in the specification of the '393
7 Patent appears to you to be an accurate
8 representation -- actually, let me ask a
9 different question.
10 Do you have a copy of the '393 Patent?
11 (Whereupon, US Patent No.
12 11,591,393 B2, dated 2-28-23 was
13 marked as Exhibit 1001 for
14 identification as of this date.)
15 A Yes, I did.
16 Q And can I turn your attention to
17 Column 1 of that patent, where it says it has
18 the title background of the invention?
19 Let me know when you have it.
20 A Yes. I have it.
21 Q Okay. And as part of your work in this
22 case, you read the background of the

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

1 sure if I recall whether they -- the fact
2 that they had recruited patients was already
3 known publicly.
4 Q And when you say they had "recruited
5 patients" are you talking about JHU and the
6 study for which JHU was the sponsor involving
7 MSI-High Pembrolizumab?
8 A I'm talking about the -- do you see the
9 text in the second to the last paragraph of
10 the background. I'll read it to you.
11 It says, to test this hypothesis --
12 MR. MILLER: Just go slowly when your
13 reading.
14 A Sorry. We initiated -- so it's in the
15 past tense, and then it said, we also
16 recruited patients, so there. It's written
17 that they did something and I don't recall
18 when that was publicly known.
19 Q Okay. So let me make sure you
20 understand my question. So I'm asking -- my
21 question relates to the July 10, 2015
22 critical date and you do understand that by

1 the July 10, 2015 critical date, there was an
2 understanding that the study has been
3 ongoing, right?
4 A I don't -- sitting here right now, I
5 would have to parse this language to
6 understand whether or not they are providing
7 information that was not yet public.
8 Q Okay. And do you know when the trial
9 results were released for the study that's
10 being described in the '393 Patent.
11 A Are you talking about the New England
12 Journal paper?
13 Q Sure.
14 A Yeah, I don't have a date in the top of
15 my head, but it would be easy to find.
16 Q Okay. So sitting here today, you don't
17 know whether or not the New England Journal
18 paper that you referred to was published
19 before July 10, 2015 or not; is that fair?
20 A No. It was published after.
21 Q Okay. Let me ask you this question, the
22 '393 Patent described the Phase II trial

1 designed to evaluate immune checkpoint
2 blockade in patients whose tumors had or did
3 not have MMR deficiency, right?
4 A That is correct.
5 Q And the Phase II clinical trial
6 described in the '393 Patent is the same
7 Phase II clinical trial announced in the
8 MSI-High study record that you talk about in
9 your declaration, right?
10 A I --
11 MR. MILLER: Could I have the question
12 back, please.
13 Q The Phase II clinical trial described in
14 the '393 Patent is the same Phase II clinical
15 trial announced in the MSI-High study record
16 that you talk about in your declaration,
17 right?
18 MR. MILLER: Objection. Form.
19 A I don't think the patent describes that
20 clinical trial. It refers to it and it
21 provides some information about it.
22 Q Well, you would agree that the MSI-High

1 study record is the initial announcement of
2 the same clinical trial later described with
3 additional details and results in the '393
4 Patent, right?
5 A My recollection is that the study record
6 was updated over time and so the actual final
7 clinical trial that was published in the New
8 England Journal and some of that data is
9 included in this patent, is a modification of
10 the original study record.
11 Q Doctor, you wrote your declaration that
12 you signed on October 4, 2024, right?
13 A Correct.
14 Q And you signed it, you understood what
15 you wrote, right?
16 A Correct.
17 Q Let me ask my question again.
18 You agree that the MSI-High study record
19 is the initial announcement of the same
20 clinical trial later described with
21 additional details and results in the '393
22 Patent, right?

1 A Yes, it is the initial announcement.
2 Q The MSI-High study record is the initial
3 announcement of the same clinical trial later
4 described with additional details and results
5 in the '393 Patent, right?
6 MR. MILLER: Objection. Asked and
7 answered.
8 A The original study record referred to a
9 trial that evolved and became the clinical
10 trial that it was -- that generated the data
11 that was provided in the '393 Patent.
12 Q And Doctor, didn't you submit sworn
13 testimony in your declaration stating:
14 "The MSI-High study record is the
15 initial announcement of the same
16 clinical trial later described with
17 additional details and results in the
18 '393 Patent"?
19 A Can you point to where in the
20 declaration that quote comes from.
21 Q We can take a look at Paragraph 67 of
22 your August 4, 2024 declaration, let me know

1 when you have it, sir?
2 A Yes. That's correct.
3 Q Let me ask my question because I want to
4 make sure it's clear.
5 You agree this MSI-High study record is
6 the initial announcement of the same clinical
7 trial later described with additional details
8 and results in the '393 Patent, right?
9 A Correct.
10 Q And to your knowledge all of the
11 figures, tables, and clinical data within the
12 '393 Patent come from that clinical trial
13 that was initially announced in the MSI-High
14 study record, right?
15 A I'm just looking at the figures, you
16 asked if all the figures are derived from the
17 clinical trial.
18 Q I'll say my question again.
19 To your knowledge all of the figures,
20 tables, and clinical data within the '393
21 Patent comes from the clinical trial that was
22 initially announced in the MSI-High study

1 record, right?
2 A Yeah, I'm just looking at the figures.
3 Q Sure.
4 A Looking at this right now I don't find
5 any figures that are not derived from that
6 clinical trial.
7 Q Okay. So that was an answer to part of
8 my question, so let me just ask the rest.
9 To your knowledge, all of the tables and
10 clinical data within the '393 Patent come
11 from that clinical trial initially announced
12 in the MSI-High study record, right?
13 A I'm just going to review the tables.
14 Q Sure.
15 A Yes. The tables are all derived from
16 the clinical trials.
17 Q Okay. And the other part of my question
18 is about the clinical data, so let me ask it
19 so we're clear.
20 To your knowledge, the clinical data
21 within the '393 Patent comes from the
22 clinical trial initially announced in the

1 MSI-High study record, right?
2 A I'm just looking at the examples.
3 That's correct.
4 Q And to your knowledge, the support for
5 the claims of the '393 Patent come from that
6 clinical trial that was initially announced
7 in the MSI-High study records, right?
8 A Correct.
9 Q Now, you read each of the '393 Patent
10 claims, right?
11 A Yes.
12 Q And there are 42 claims in the '393
13 Patent, right?
14 A Correct.
15 Q And you understood every one of those 42
16 claims when you read them, right?
17 A Correct.
18 Q You were not confused by anything
19 written in those 42 claims, right?
20 A I was not confused.
21 Q If asked you could explain the meaning
22 of any language in those claims, right?

1 A Correct.
2 Q Now, Claim 1 of the '393 Patent is a
3 method of treating MSI-High colorectal cancer
4 in a human patient, right?
5 A Correct.
6 Q You understand that clinical oncologists
7 treat cancer patients, right?
8 A Correct.
9 Q Do you believe that a clinical
10 oncologist would need specialized experience
11 researching and or developing new treatment
12 for cancer for that clinical oncologist to
13 understand the steps of the method of
14 Claim 1?
15 A No.
16 Q You would agree the method in Claim 1 of
17 the '393 Patent, is a cancer patient
18 treatment method and not a method for
19 conducting immunology research, right?
20 A Correct.
21 Q You would agree the method in the
22 Claim 1 is a cancer treatment method and not

1 a method for conducting genetic research,
2 right?
3 A Correct.
4 Q Claims 2 through 13 of the '393 Patent
5 are methods of treating MSI-High colorectal
6 cancer in a human patient, right?
7 A Correct.
8 Q Claims 31 through 42 are methods of
9 treating MSI-High colorectal cancer in a
10 human patient, right?
11 A Correct.
12 Q You would agree that the methods in
13 Claims 2 to 13, 31 through 42 of the '393
14 Patent are cancer patient treatment methods
15 and not methods for conducting immunology
16 research, right?
17 A Correct.
18 Q You would agree that the methods in
19 Claims 2 to 13, 31 to 42 of the '393 Patent
20 are cancer patient treatment methods and not
21 methods for conducting genetics research,
22 right?

1 A Correct.
2 Q Turning your attention to Claim 14,
3 Claim 14 of the '393 Patent, is a method of
4 reducing the risk of cancer progression or
5 increasing overall survival in a human
6 patient who has MSI-High colorectal cancer
7 patients, right?
8 A Correct.
9 Q You would agree that part of the duty of
10 a clinical oncologist is to attempt to reduce
11 the risk of cancer progression in cancer
12 patients under their care, right?
13 A Correct.
14 Q You would agree that part of the duty of
15 clinical oncologists is to attempt to
16 increase overall survival in a human patient
17 under their care who have cancer, right?
18 A Correct.
19 Q Do you believe that a clinical
20 oncologist would need specialized experience
21 researching and/or developing new treatments
22 for cancer to understand the method of

1 Claim 14 of the '393 Patent?
2 A Could you repeat the question?
3 Q Sure.
4 Do you believe that a clinical
5 oncologist would need specialized experience
6 researching and/or developing new treatments
7 for cancer to understand the method of
8 Claim 14 of the '393 Patent?
9 A No.
10 Q You would agree that the methods in
11 Claim 14 of the '393 Patent are cancer
12 patient treatment methods and not methods for
13 conducting immunology research, right?
14 A Correct.
15 Q You would agree that the methods in
16 Claim 14 are cancer patient treatment methods
17 and not methods for conducting genetics
18 research, right?
19 A Correct.
20 Q Turning your attention to Claims 15
21 through 30 of the '393 Patent. Doctor,
22 Claims 15 through 30 are methods of reducing

1 the risk of cancer progression or increasing
2 overall survival in a human patient who has
3 MSI-high colorectal cancer, right?
4 A Correct. They're all dependent on
5 Claim 14.
6 Q Okay. And you would agree that the
7 methods in Claims 15 through 30 of the
8 '393 Patent are cancer patient treatment
9 methods and not methods for conducting
10 immunology research, right?
11 A Correct.
12 Q And you would agree that the methods in
13 Claims 15 through 30 of the '393 Patent are
14 cancer patient treatment methods and not
15 methods for conducting genetics research,
16 right?
17 A Correct.
18 Q Now, let me turn your attention to
19 Claim 1 of the '393 Patent. Let me know when
20 you have it, sir.
21 A I have it.
22 Q Do you see that the claim method of

1 Claim 1 contains a step of "testing, or
2 having tested, a biological sample obtained
3 from a patient having colorectal cancer,
4 thereby determining that the patient's
5 colorectal cancer is microsatellite
6 instability high or DNA mismatch repair
7 deficient"?
8 A Correct.
9 Q And do you see that Claim 1 of the
10 '393 Patent also contains a step of "in
11 response to determining that the colorectal
12 cancer is microsatellite instability high or
13 DNA mismatch repair deficient, treating the
14 patient with a therapeutically effective
15 amount of pembrolizumab"?
16 A Correct.
17 Q Other than those two steps that we've
18 just discussed, are there any other steps of
19 the method recited in Claim 1?
20 A Those are the two steps.
21 Q Okay. Now, would you agree that giving
22 a MSI-High colorectal cancer patient

1 10 milligrams per kilogram of pembrolizumab
2 every 14 days is an effective amount of
3 pembrolizumab as required by Claim 1 of the
4 '393 Patent?
5 MR. MILLER: Objection. Form.
6 A Could you repeat the dosing?
7 Q Let me repeat my question 'cause I want
8 to make sure there's clarity in the record.
9 I'll try to slow down when I get to the
10 dosing.
11 Would you agree that giving a MSI-High
12 colorectal cancer patient 10 milligrams per
13 kilogram of pembrolizumab every 14 days is an
14 effective amount of pembrolizumab as required
15 by Claim 1 of the '393 Patent?
16 A Yeah, I just want to go back to the
17 examples. In Example 2, "The study agent,
18 pembrolizumab, was administered at 10 mg/kg
19 intravenously every 14 days." So that's a
20 correct recitation of the specification.
21 Q Okay. And Doctor, based on your careful
22 read of the '393 Patent, the only dose of

1 pembrolizumab recited in the patent is
2 10 milligrams per kilogram every 14 days,
3 right?
4 A I would have to go back to the
5 specification and read it through to make
6 sure that there's no additional references or
7 not.
8 Q Okay. So sitting here today right now,
9 you don't have an understanding whether or
10 not beyond 10 milligrams per kilogram every
11 14 days there's a different dosing regimen of
12 pembrolizumab recited in the '393 Patent; is
13 that fair?
14 A I don't remember if additional dosing
15 regimens are recited or not in the
16 specification.
17 Q Okay. Now, Doctor, based on your
18 understanding of Claim 1, does the language
19 "effective amount of pembrolizumab," in
20 Claim 1 include any amount of pembrolizumab
21 beyond the 10 milligrams per kilogram every
22 14 days that you remember that's recited in

1 the '393 Patent?
2 MR. MILLER: Objection. Form.
3 A I think the language in the claim is
4 quite clear. It says "a therapeutically
5 effective amount." So whatever amount is
6 therapeutically effective would be included
7 under the claim. And there are a number of
8 different dosing regimens for pembrolizumab,
9 including now a hyaluronidase coformulation,
10 that is a different but also effective amount
11 of pembrolizumab.
12 Q Okay. So sitting here today, it's your
13 understanding that when Claim 1 recites
14 "effective amount of pembrolizumab," that can
15 include amounts of pembrolizumab beyond the
16 "10 milligram per kilogram every 14 days"
17 regimen that you recall as being recited in
18 the '393 Patent; is that fair?
19 A When you say "beyond," are you saying a
20 greater amount?
21 Q Any additional amount.
22 A Any additional beyond 10 milligrams? So

1 added to, like 11?
2 Q No. Let me try my question again.
3 Based on your understanding of the
4 language in Claim 1 that says "effective
5 amount of pembrolizumab," is it your belief
6 that an effective amount of pembrolizumab
7 could be a dosing regimen other than the
8 10 milligrams per kilogram every 14 days
9 that's recited in the '393 Patent?
10 A I think the language is quite clear.
11 It's whatever is an effective amount. And it
12 was known, and in fact incorporated by
13 reference in the patent, that there are other
14 amounts of pembrolizumab where activity had
15 been seen in other cancers. So I think it's
16 inherent within the specification that
17 10 milligrams per kilogram every 14 days is
18 not a limitation.
19 Q Do you know whether or not the
20 specification actually identifies any dosing
21 regimen for pembrolizumab other than
22 10 milligrams per kilogram every 14 days?

1 A Well, the specification includes
2 53 references, and my memory is that some of
3 those references include clinical trials that
4 had explored different doses. I would have
5 to go back and look at those references to
6 make sure that my recollection is correct.
7 Q And any of those 53 references that
8 you're talking, are any of them references
9 where pembrolizumab was given to a MSI-High
10 colorectal cancer patient?
11 A I would have to go back and go through
12 the references.
13 Q And sitting here today, you just don't
14 know, right?
15 A I don't recall, but I do think that
16 other dosing regimens would be inherent and
17 that anyone reading the claim would
18 understand that there are different dosing
19 regimens that are possible. For example,
20 dosing higher and less frequently or lower
21 and more frequently would provide for the
22 same coverage.

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

1 You understand that the recommended
2 dosage of KEYTRUDA for the MSI-High
3 indications and its package insert are
4 different from the "10 milligram per kilogram
5 every 14 day" dosing regimen that you recall
6 being recited in the '393 Patent, right?
7 A It's to me irrelevant because all that's
8 important is what is -- what is the PK. Do
9 you get a similar coverage of your drug in
10 the blood with a different dosing regimen? I
11 think that's inherent, and anyone skilled in
12 the art would understand that.
13 Q So I understand you have positions,
14 Doctor, but I'd like an answer to my
15 question.
16 And so my question is you understand
17 that the recommended dosage for giving
18 KEYTRUDA to MSI-High phenotypes in the
19 package insert is different from the
20 "10 milligrams per kilogram every 14 day"
21 regimen that you recall being cited in the
22 '393 Patent, right?

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

1 demonstrating that since the conclusion of
2 the clinical trial described in the MSI-High
3 study records, any clinical oncologist has
4 ever prescribed KEYTRUDA to a MSI-High
5 patient in the amount of 10 milligrams per
6 kilograms every 14 days?
7 A There is no database that covers how
8 every patient is treated. There's no way
9 that anyone could know the answer to that
10 question.
11 Q Doctor, I'm not asking you about anyone.
12 I'm not asking you about a database. I'm
13 asking specifically about you.
14 Doctor, are you aware of any evidence
15 demonstrating that since the conclusion of
16 the clinical trial described in the MSI-High
17 study records, any clinical oncologist has
18 ever prescribed KEYTRUDA to an MSI-High
19 patient in the amount of 10 milligrams per
20 kilograms every 14 days? If you're not
21 aware, you could just say that.
22 MR. MILLER: Objection. Form. Asked

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

1 tissue or bodily fluid could be tested,
2 right?
3 A Correct. The standard procedure is
4 tumor tissue. Bodily fluid requires a more
5 specialized assay.
6 Q And at the time of the critical date,
7 July 10, 2015, you would agree that testing a
8 patient for MSI status could be accomplished
9 by carrying out a PCR test, right?
10 A That was the initial standard assay for
11 MSI-High, but at the time of the critical
12 date, it was being overtaken by a different
13 assay.
14 Q Okay. Doctor, I'm not asking about
15 what's the initial standard. I'm asking a
16 different question, and it's this: At the
17 time of the critical date, July 10, 2015, you
18 would agree that testing a patient for
19 MSI-High status could be accomplished by
20 carrying out a PCR test, right?
21 A Yes. "Could" is the critical part of
22 that answer, yes.

1 Q I didn't say anything different.
2 So, Doctor, at the time of the critical
3 date, July 10, 2015, you would agree that
4 testing a patient for MSI-High status could
5 be accomplished by carrying out a
6 next-generation sequencing on a sample,
7 right?
8 MR. MILLER: I'm sorry. Could I have
9 the question back?
10 Q At the time of the critical date,
11 July 10, 2015, you would agree that testing a
12 patient for MSI-High status could be
13 accomplished by carrying out a
14 next-generation sequencing test on a sample,
15 right?
16 A I would have to refresh my memory as to
17 the availability of that particular assay.
18 Q Okay. Sitting here today, you don't
19 know if that assay was available before
20 July 10, 2015, right? Is that fair?
21 A That's fair.
22 Q Okay. Would you agree that at the time

1 of the critical date, testing a patient for
2 MSI-High status could be established by
3 carrying out an immunology history chemistry
4 test?
5 MR. MILLER: Objection. Form.
6 A Yes. That was probably the most
7 frequently employed assay at the critical
8 date.
9 Q The JHU-named inventors on the
10 '393 Patent were not the first persons to
11 test a biological sample to determine if a
12 cancer patient is MSI-High, right?
13 A That's correct.
14 Q The JHU-named inventors on the
15 '393 Patent did not invent testing a
16 biological sample to determine if a cancer
17 patient is MSI-High, right?
18 A That's correct.
19 Q The JHU-named inventors were not the
20 first persons to use a PCR test to determine
21 if a cancer patient was MSI-High, right?
22 A That's correct.

1 Q The JHU-named inventors of the
2 '393 Patent were not the first persons to use
3 next-generation sequencing to determine if a
4 cancer patient was MSI-High, right?
5 A That's correct.
6 Q The JHU inventors of the '393 Patent
7 were not the first persons to use an
8 immunohistochemistry test to determine if a
9 cancer patient was MSI-High, right?
10 A That's correct.
11 Q The JHU-named inventors of the
12 '393 Patent did not invent using PCR to carry
13 out testing to determine MSI-High status,
14 right?
15 A That is correct.
16 Q The JHU-named inventors of the
17 '393 Patent did not invent using
18 next-generation sequencing to carry out
19 testing to determine MSI-High status, right?
20 A That is correct.
21 Q The JHU-named inventors of the
22 '393 Patent did not invent using an

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

1 A No.
2 Q Doctor, are you being paid for your work
3 on this case?
4 A Yes.
5 Q How much are you being paid?
6 A I don't recall.
7 Q Sitting here today, you don't have a
8 recollection how much you're being paid for
9 your work on this case?
10 A It's chump change. I'm not doing this
11 for the money. It doesn't -- the amount of
12 money I'm making off this case is a trivial
13 component of my income.
14 Q And, Doctor, you understand I didn't ask
15 anything about your income or whether or not,
16 how much money you are making off this case,
17 how it related to your income.
18 You understand that, right?
19 A I'm sorry. What's the question?
20 Q Sure. The question is, do you
21 understand that in my questions about how
22 much you were being compensated, I'm not

1 asking how much your compensation relates to
2 your income.
3 Do you understand that?
4 A Okay.
5 Q So let me try a different question.
6 Are you charging in this case for your
7 work by hour or --
8 A Yes.
9 Q -- or what is the arrangement that you
10 have?
11 A I'm billing per hour.
12 Q You're billing per hour?
13 A Yes.
14 Q And sitting here today, you have no idea
15 how much you're billing per hour?
16 A I don't recall, no.
17 Q And how much you're billing per hour, is
18 that reflected in some agreement that you
19 have?
20 A Yes.
21 Q With JHU?
22 A Yes.

1 Q And what agreement is that?
2 A It is an agreement with Fish &
3 Richardson.
4 Q Okay. And how many hours approximately
5 have you spent working on this case?
6 A I don't recall.
7 Q Do you have a standard rate for
8 consulting in patent cases?
9 A I don't have a single rate, no, but my
10 recollection is that I am billing John
11 Hopkins or billing Fish & Richardson less
12 than what I have billed in the past. I
13 again, I'm not doing this for the money.
14 Q And, sir, you understand, I didn't ask
15 if you were doing this for the money. You
16 understand that, right?
17 A Okay.
18 Q So my question is, do you know how many
19 hours you've spent so far on this case?
20 A I don't recall.
21 Q Sitting here today, you have no idea how
22 much time you've spent working on this case,

1 is that fair?
2 A I don't have a recollection.
3 Q Okay. Now, turning to Claim 14 of the
4 '393 Patent. Let me know when you're there,
5 sir.
6 A Okay.
7 Q Would you agree with me that Claim 14 of
8 the '393 Patent only contains two steps to
9 accomplish the method recited in Claim 14?
10 A Yes. There are two steps that are
11 recited in that claim.
12 Q Right. And the first step that's
13 recited in the claim is testing or having
14 tested a biological sample obtained from a
15 patient having colorectal cancer, thereby
16 determining that the patient's colorectal
17 cancer is Microsatellite Instability-High or
18 mismatch repair deficient, right?
19 A That's correct.
20 Q And the second step in Claim 14 of the
21 '393 Patent is:
22 "In response to determining that

1 the colorectal cancer is Microsatellite
2 Instability-High or DNA mismatch repair
3 deficient, treating the patient with a
4 therapeutically effective amount of
5 pembrolizumab," right?
6 A That's correct.
7 Q Now I'd like to turn your attention to
8 Claims 31, 33 and 35 in the '393 Patent.
9 Let me know you have it, sir.
10 A Yes. I have it.
11 Q Do you agree that Claims 31, 33 and 35
12 of the '393 Patent, each refer to method
13 results?
14 A Yes.
15 Q And would you agree that those
16 Claims 31, 33 and 35 do not recite any
17 additional steps from the two steps we talked
18 about in Claim 1 of the '393 Patent?
19 MR. MILLER: Objection, form.
20 A Well, determining an objective response
21 is a radiologic end point. And so that's an
22 additional step.

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

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

1 the '393 Patent?
2 A Well, my answer would be the same as for
3 Claim 33 and 31, in that there is a
4 determination of progressions, that is an
5 additional step.
6 Q Would you agree that Claim 35 doesn't
7 include the word "determining" anywhere in
8 the claim?
9 A Again, it's inherent.
10 Q I didn't ask you if it was inherent.
11 I'm asking you, do you see the word
12 "determining" in Claim 35 of the '393 Patent?
13 A The word "determining" is not in that
14 claim.
15 Q Okay. Now, is it your belief for
16 someone to practice the methods of Claim 31,
17 33, and 35, that they actually have to
18 determine the objective response rate and
19 determine the probability of progression-free
20 survival to practice those claims?
21 MR. MILLER: Objection to the form of
22 the question.

1 A You would practice a claim as described
2 in Claim 1. And then, to understand whether
3 or not you're falling under 35, you would
4 require that additional step of determining
5 either response or progression.
6 Q So let me make sure we're clear.
7 To understand whether or not someone
8 were practicing the methods of Claims 31, 33
9 and 35, it's your belief that you would have
10 to have evidence that the person actually
11 determined the objective response rate, and
12 determined the probability of
13 progression-free survival?
14 MR. MILLER: Object to the form of the
15 question.
16 A The way you phrased that was a little
17 bit inelegant, because you have to -- a
18 determination would have to be made to know
19 whether or not there was progression-free
20 survival or response.
21 Q Okay. So let's take it claim by claim
22 because I want to make sure I understand you.

1 Are you saying that for Claim 31, in
2 order for someone to practice that claim,
3 they actually have to do a determination of
4 the objective response rate; is that fair?
5 MR. MILLER: Objection to the form of
6 the question.
7 A To know whether or not the claim covered
8 the method, you would have to determine
9 objective response rate.
10 Q Are you finished with the answer?
11 A Yes.
12 Q Right. So to know whether or not if
13 your activity is covered by Claim 31, you
14 would actually have to determine the
15 objective response rate; is that right?
16 MR. MILLER: Objection to the form of
17 the question.
18 A That's correct.
19 Q Okay. And Claim 31 refers to colorectal
20 cancer patients in the plural. As you
21 understand it, who are these -- who is this
22 group of patients in the plural?

1 A The patients who are being treated.
2 Q Is that every patient in the United
3 States?
4 MR. MILLER: Objection, form.
5 A I don't think there's a territorial
6 limitation.
7 Q So to be covered under this claim, you
8 would have to do a determination of objective
9 response rate based upon every colorectal
10 cancer patient that's been treated. Is that
11 what you're saying?
12 MR. MILLER: Objection to the form of
13 the question.
14 A No.
15 Q So what's a group of colorectal cancer
16 patients that you would have to make this
17 objective response rate determination on --
18 A A --
19 Q -- in using Claim 31? Go ahead.
20 MR. MILLER: Objection to the form of
21 the question.
22 A A statistically significant number of

1 patients.
2 Q And how many patients is that?
3 MR. MILLER: Objection to the form of
4 the question.
5 A I'm not a statistician.
6 Q So sitting here today, you don't how
7 many patients you would need to treat and to
8 be covered under the method of Claim 31; is
9 that fair?
10 MR. MILLER: Objection, form.
11 A I would have to do some work to
12 determine that.
13 Q And looking at Claim 33, it also refers
14 to colorectal cancer patients in the plural.
15 Do you see that?
16 A Yes.
17 Q And how many colorectal cancer patients
18 does this claim refer to, as you understand?
19 MR. MILLER: Objection, form.
20 A A statistically significant number of
21 patients.
22 Q And how many patients is that for

1 Claim 33 of the '393 Patent?
2 MR. MILLER: Objection, form.
3 A Again, I would have to do some work to
4 determine that.
5 Q You haven't determined that as part of
6 your work in this case so far, right?
7 A I don't recall. The number of patients
8 that were analyzed in the clinical trial was
9 enough to provide statistical significance
10 for end points like progression-free survival
11 or objective response rate, but I don't
12 recall at what week that statistical
13 significance falls off.
14 Q I'm asking a different question.
15 In your work in this case, did you
16 determine how many colorectal cancer patients
17 would need to be treated to be covered under
18 the method of Claim 33?
19 MR. MILLER: Objection, form.
20 A I read the New England Journal paper,
21 and my opinion is that the statistical
22 analysis was correct in that paper.

1 Q So, Doctor, I didn't ask you if you read
2 the New England Journal of Medicine paper.
3 And I didn't ask you if the statistical
4 analysis in that paper was correct. My
5 question is very different.
6 I'm asking you, Doctor, as part of your
7 work in this case, did you ever make a
8 determination as to how many colorectal
9 cancer patients someone would need to treat
10 to be covered under Claim 33 of the '393
11 Patent?
12 MR.MILLER: Objection, form.
13 Q Did you ever do that?
14 A I don't recall.
15 Q Now, looking at Claim 35, you see that
16 claim also refers to colorectal cancer
17 patients in the plural, right?
18 A Correct.
19 Q Did you ever do any work in this case to
20 determine how many colorectal cancer patients
21 someone would need to treat to be covered by
22 Claim 35 of the '393 Patent?

1 MR. MILLER: Objection, form.
2 A I don't recall.
3 Q Now, with respect to -- let me turn your
4 attention to Claims 37, 39 and 41.
5 Do you agree that each of those claims
6 refer to method results?
7 A Yes.
8 Q And do you agree that those claims do
9 not recite any additional steps from the two
10 steps that we talked about in Claim 29 of the
11 '393 Patent?
12 MR. MILLER: Objection, form.
13 A The additional step would be a
14 determination of either response rate or
15 progression.
16 Q So for Claims 37, 39 and 41, it's your
17 belief that there's an additional step of
18 determining objective response rate or
19 probability of progression-free survival,
20 even though the claims do not contain the
21 word "determining"; is that fair?
22 MR. MILLER: Objection, form.

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

1 because it was a rather long multi-part
2 question.
3 Q Sure. Let's look at Claim 37.
4 With respect to Claim 37, do you believe
5 to be covered by that claim, you would
6 actually have to make a determination of what
7 is the objective response rate on a group of
8 colorectal cancer patients that were treated?
9 MR. MILLER: Objection. Form. Scope.
10 A To understand whether or not Claim 37 is
11 relevant you would need to have an objective
12 response rate determination made.
13 Q What do you mean by to understand if
14 Claim 37 is relevant?
15 A Whether it covers the method of the
16 invention.
17 Q So my question is to understand whether
18 or not you're actually practicing Claim 37
19 and covered by that method, does the person
20 actually have to do a determination of the
21 objective response rate based upon a group of
22 colorectal cancer patients?

1 MR. MILLER: Objection. Form and
2 scope.
3 A Who's the person you're referring to?
4 Q Well, Doctor, in your declaration you
5 make the claim that an oncologist prescribing
6 KEYTRUDA to a colorectal cancer patient under
7 the colorectal related indication described
8 on the package insert would necessarily
9 practice the method of treatment claimed in
10 at least Claim 1 of the '393 Patent, right,
11 do you remember that?
12 A Can you tell me where in the declaration
13 that is?
14 Q Sitting here right now, you don't
15 remember saying that in your declaration?
16 A I can find it pretty easily. Let me
17 look in the index.
18 Q Well, I didn't ask you to go find it.
19 I'm asking you, sitting here right now, do
20 you remember saying that, yes or no?
21 A Okay. To answer the question, I'm going
22 to right now look through the index and I'm

1 going to go now towards the end of my
2 declaration and, I believe that what you're
3 referring to is at -- is close to the end of
4 the declaration, so I'm just trying to get
5 there. I think I'm pretty close to it, I'm
6 getting there.
7 Q Let me extend my question. Without
8 looking at your declaration do you understand
9 that --
10 A You don't want me look at my
11 declaration?
12 MR. MILLER: Let him finish, go ahead.
13 Q That's right. Right now my question is
14 focused on this.
15 Without looking at your declaration and
16 sitting here today, do you have any
17 recollection giving sworn testimony, that an
18 oncologist prescribing KEYTRUDA to a
19 colorectal cancer patient under the
20 colorectal related indication described in
21 the package insert would necessarily practice
22 the method of treatment claimed in at least

1 Claim 1 of the '393 Patent?
2 MR. MILLER: Objection. Form.
3 Q Yes or no?
4 A My recollection is that is what I wrote,
5 but to check that and make sure given that
6 there's a lot of words in the declaration, I
7 would like to look at the exact words, in
8 which my memory is very close to the end of
9 my declaration it would be very easy for me
10 to look at that.
11 Q That's fine. My question is focused on
12 something different. Now I appreciate what
13 your state of mind right now and your current
14 recollection.
15 So if you could, Doctor, turn to
16 Paragraph 190 of your declaration, and let me
17 know when you have it. And this is your
18 October 4, 2024 declaration.
19 A Yes. That's correct.
20 Q So my question for you is: You say at
21 least Claim 1 of the '393 Patent in
22 Paragraph 190 of your declaration, other than

1 Claim 1, are there any additional claims that
2 you believe would be necessarily practiced by
3 the method of treatment -- sorry, let me
4 start over.
5 Other than Claim 1 of the '393 Patent,
6 do you believe that there would be any other
7 methods necessarily practiced if an
8 oncologist is prescribing KEYTRUDA to a CRC
9 patient under the CRC related indications in
10 the package insert?
11 MR. MILLER: Objection. Form.
12 A I would have to go back and do some work
13 to identify which are the relevant claims.
14 Q I'm not sure if I asked -- I'm not
15 asking about the relevant claims.
16 In your declaration you say that if an
17 oncologist is following the package insert,
18 they would necessarily practice the method of
19 treatment claimed in at least Claim 1 of '393
20 Patent.
21 So my question is: Beyond Claim 1, are
22 there any additional claims in the '393

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

1 which claims are relevant.
2 Q Okay. And you haven't done that work so
3 far in this case, right?
4 A I think my recollection is I have. But
5 I don't recall the determination that I made.
6 Q So you believe that you had made a
7 determination looking at the 42 claims in the
8 '393 Patent whether or not an oncologist
9 would necessarily be practicing the method of
10 the '393 Patent?
11 A That is my recollection.
12 Q Okay. Let's take a look at one.
13 Looking at Claim 31 of the '393 Patent.
14 Let me know when you have that?
15 A Yes, I do.
16 Q And do you believe if an oncologist
17 followed the method -- strike that.
18 Do you believe if an oncologist followed
19 the prescribing, the recommended prescribing
20 method for CRC patient under the CRC related
21 indications in the package insert that the
22 oncologist would necessarily be practicing

1 treatment method of Claim 31?
2 MR. MILLER: Objection. Form and
3 scope.
4 A I would have to do a little bit of work.
5 Q Sitting here today, do you know, do you
6 have an opinion?
7 A I'd have to do a little bit of work.
8 Q Sitting here today, do you have an
9 opinion, if you know?
10 A Again, I would have to do a little bit
11 of work to do that, to determine that.
12 Q I just want to make sure I'm clear.
13 Sitting here today, do you know with respect
14 to Claim 31?
15 A I don't recall.
16 Q Do you know with respect to Claim 33?
17 A Again, I would have to do some work. I
18 don't recall my determination on the
19 individual claims.
20 Q And did you make a determination with
21 respect to Claim 35?
22 A Yes.

1 Q And is it your opinion, that if an
2 oncologist prescribes KEYTRUDA according to
3 the CRC-related indication in the package
4 insert, the oncologist would necessarily be
5 practicing the method of Claim 35 of this
6 '393 Patent?
7 MR. MILLER: Objection. Form and
8 scope.
9 A I don't recall my determination.
10 Q Do you recall your determination for
11 that same question as to Claim 7 of the '393
12 Patent?
13 MR. MILLER: Objection. Form and
14 scope.
15 A I don't recall.
16 Q And do you recall if you made a
17 determination with respect to that same
18 question as to Claim 39 of the '393 Patent?
19 MR. MILLER: Objection. Form and
20 scope.
21 A I don't recall.
22 Q Do you recall with respect to that same

1 question, if you made a determination with
2 respect to Claim 31 of the '393 Patent?
3 MR. MILLER: Objection. Form and
4 scope.
5 A I recall I made a determination I may
6 have answered the previous question too
7 quickly because I also recall that I made a
8 determination. I just don't recall the
9 results of that determination.
10 Q And if you made that determination,
11 would it be in your declaration?
12 A Not necessarily.
13 Q Okay. So it could be something that
14 you're just not testifying to, right?
15 A Not all the determinations that I made
16 are in the declaration, no.
17 Q All right. I want to just be sure we're
18 really clear about this. Turning your
19 attention to Paragraph 190 of your
20 declaration and your statement where you say
21 an oncologist prescribes KEYTRUDA to CRC
22 patient under the CRC-related indications

1 described above would necessarily practice
2 the method of treatment claimed in at least
3 Claim 1 of the '393 Patent, sitting here
4 today, can you name any claim, other than
5 Claim 1, that you're talking about in that
6 space?
7 MR. MILLER: Objection. Form and
8 scope.
9 A I don't recall, no.
10 Q Now, the determination steps that you
11 believe is in Claim 31, 33, 35, 37, 39, and
12 41 of the '393 Patent, were those steps to
13 make that determination in your view known
14 publicly as of the July 10, 2015 critical
15 date?
16 A Yes. And they're also clearly disclosed
17 in the specification.
18 Q Now, looking again at Claims 31, 33, 35,
19 37, 39, and 41 of the '393 Patent, you
20 understand that each of those claims refer to
21 colorectal cancer patients in the plural,
22 right?

1 A Correct.
2 Q And would you agree that an objective
3 response rate would not apply to a single
4 patient that's treated?
5 MR. MILLER: Objection. Form.
6 A It would apply, it just wouldn't be
7 determinable from a single patient.
8 Q Okay. So you would agree that you could
9 not determine an objective response rate if
10 you only treated a single patient; is that
11 fair?
12 MR. MILLER: Objection. Form.
13 A That's correct.
14 Q And is it also fair that the probability
15 of progression-free survival at 20 weeks
16 would also not be determinable if you were
17 only treating a single patient?
18 MR. MILLER: Objection. Form.
19 A That's correct.
20 Q And would you agree with respect to
21 these claims that the probability of
22 progression-free survival could also not be

1 determined if you were only treating a single
2 colorectal cancer patient?
3 MR. MILLER: Objection. Form.
4 A That's correct.
5 Q Now, as part of your work on this case
6 you reviewed the MSI-High study record,
7 right?
8 A Yes.
9 Q And you understand that before the
10 critical date the study record was posted
11 publicly in clinicaltrials.gov, right?
12 A Correct.
13 Q You reviewed the study record carefully,
14 right?
15 A Correct.
16 Q And you reviewed the study record
17 objectively, right?
18 A Correct.
19 Q You reviewed the study record without
20 any bias whatsoever, right?
21 A Correct.
22 Q And JHU's counsel informed you that you

1 should consider the study record through the
2 lens of one of ordinary skill in the art at
3 the time of the July 10, 2015 critical date,
4 right?
5 A Correct.
6 Q And did you consider the study record
7 with that lens?
8 A Yes.
9 Q And do you believe that you understand
10 how a person of ordinary skill would have
11 read and understood the study record?
12 A Correct.
13 Q And you would agree that the person of
14 ordinary skill would not read the study
15 record with any bias, right?
16 A Correct.
17 Q And you would agree that the person of
18 ordinary skill would not read the study
19 record in an illogical way, right?
20 A Correct.
21 Q And you understand that all prior art
22 references such as the posted study records,

1 are to be looked at from the viewpoint of the
2 person of ordinary skill in the art, right?
3 A Correct.
4 Q And would you agree that if the person
5 of ordinary skill set out to conduct the
6 clinical trial disclosed in the study record,
7 the person of ordinary skill would perceive
8 rationally, right?
9 MR. MILLER: Objection. Form.
10 A Correct.
11 Q You would agree that if the person of
12 ordinary skill set out to conduct a clinical
13 trial disclosed in the study record, a person
14 of ordinary skill would proceed logically,
15 right?
16 MR. MILLER: Objection. Form.
17 A Correct.
18 Q And you understand that the person of
19 ordinary skill has ordinary creativity,
20 right?
21 MR. MILLER: Objection. Form.
22 A Correct.

1 Q And you understand that the person of
2 ordinary skill can make inferences and
3 creative steps, right?
4 A Correct.
5 Q And you understand that the person of
6 ordinary skill has ordinary creativity and is
7 not an automaton, right?
8 A Correct.
9 Q And you would agree that the person of
10 ordinary skill does not doubt the literature
11 that that person reads, right?
12 MR. MILLER: Objection. Form.
13 Go ahead.
14 A I think a person of ordinary skill in
15 the art reads the literature skeptically,
16 always.
17 Q Right. So it's your belief that the
18 person of ordinary skill, when that person
19 reads the literature, they're reading it
20 skeptically; is that fair?
21 A The person of ordinary skill in the art
22 would be a scientist, and scientists always

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

1 but I'm also aware of the way "distrustful"
2 shows up in the English language. And so I'm
3 a little concerned that you might not be
4 capturing the skeptical lens that is part of
5 the scientific method.
6 Q Right. And for your work in this case,
7 when you view the prior art from the
8 perspective of the person of ordinary skill
9 in the art, you applied a skeptical lens; is
10 that right?
11 A Well, when I read the prior art, I read
12 it trying to consider what a person of
13 ordinary skill in the art would -- how a
14 person of ordinary skill in the art would
15 read that particular reference, that
16 particular piece of prior art, whether or not
17 they would take it at face value or not.
18 Q Right. And from your perspective, a
19 person of ordinary skill in the art would
20 naturally have a skeptical lens when looking
21 at a piece of prior art; is that fair?
22 A A person of ordinary skill in the art

1 would have a skeptical lens when viewing
2 any -- any scientific publication.
3 Q Okay. And would you agree that the
4 person of ordinary skill in the art would
5 have seen a trial disclosed in the study
6 record that you discussed in your
7 declaration, right?
8 A A person of ordinary skill in the art
9 would have viewed that as a disclosure that a
10 trial will take place. The person of
11 ordinary skill in the art would understand
12 that that is a regulatory requirement to post
13 that study record.
14 Q But you understand that the person of --
15 well, let me ask you.
16 Would you agree that the person of
17 ordinary skill in the art would have seen a
18 trial disclosed in the study record?
19 MR. MILLER: Objection. Asked and
20 answered.
21 A Again, I thought I answered that. It's
22 a disclosure of a trial that will take place,

1 that is planned to take place.
2 Q Well, you believe that there was a trial
3 disclosed in the MSI-High study record,
4 right?
5 A Yes.
6 Q And so would you agree that the --
7 A It was a disclosure of a trial that
8 would take place.
9 Q Let me try this again.
10 You agree that there was a trial
11 disclosed in the MSI-High study record,
12 right?
13 MR. MILLER: Objection. Asked and
14 answered.
15 A Again, I thought I answered that. That
16 trial was a planned trial, yes.
17 Q So you agree that there was a trial
18 disclosed in the MSI-High study record,
19 right?
20 MR. MILLER: Objection. Asked and
21 answered.
22 A Yeah, the trial was planned, so I agree

1 with you.
2 Q And you agree that the POSA would have
3 seen a trial disclosed in the study record,
4 right?
5 A They would have seen that a trial was
6 planned, yes, from the study record, so I
7 agree.
8 Q And the POSA would understand that the
9 trial is a Phase II study of the chemical
10 compound MK-3475 in patients with
11 microsatellite unstable tumors, right?
12 MR. MILLER: Objection. Form.
13 A My recollection is, yes, that's correct.
14 Q And MK-3475 is pembrolizumab, right?
15 A That's correct.
16 Q And the POSA would have seen in that
17 study record that one of the steps for
18 conducting the study is giving 10 milligrams
19 per kilogram of pembrolizumab every 14 days
20 to microsatellite instability-high colorectal
21 cancer patients, right?
22 A I don't have the study record in front

1 of me. That sounds reasonable. But if you'd
2 like me to confirm that, perhaps we could
3 pull up the study record.
4 Q Sure. Let's bring up the study record.
5 It's Exhibit 1005.
6 (Whereupon, Study NCT01876511,
7 dated 6-10-13 was marked as
8 Exhibit 1005 for identification
9 as of this date.)
10 Q I think we can get help putting it in
11 the chat, and then you can download it, sir.
12 TECH WELCH: This is the remote tech.
13 Exhibit 1005, it's uploading to the
14 shared folder now.
15 Q Just let me know when you have it, sir.
16 TECH WELCH: And please be mindful
17 that you may need to refresh the page.
18 A Okay. I have it.
19 Q Okay. Now, the POSA would have seen
20 that one of the steps for conducting the
21 study is giving 10 milligrams per kilogram of
22 pembrolizumab every 14 days to MSI-High

1 colorectal cancer patients, right?
2 A That is a component of the trial. That
3 is one of the cohorts.
4 Q Okay. And at the time of the invention
5 of the '393 Patent -- and this is the
6 July 10, 2015 date -- as you understand it,
7 it was known that a small percentage of
8 cancer patients were MSI-High, right?
9 A My recollection --
10 MR. MILLER: Sorry.
11 Objection. Form.
12 Go ahead.
13 A My recollection is that at the time of
14 the invention at July 10th, 2015, that the
15 published numbers for the percentage of
16 colorectal cancer patients that were MSI-High
17 was in the range of 15 percent.
18 Q And so would you agree that at the time
19 of the invention of the '393 Patent, it was
20 known that a small percentage of cancer
21 patients were MSI-High?
22 MR. MILLER: Objection. Form.

1 A My recollection is that the numbers were
2 around 15 percent.
3 Q And so I'm asking you would you agree
4 that at the time of the invention of the
5 '393 Patent, it was known that a small
6 percentage of cancer patients were MSI-High.
7 MR. MILLER: Objection. Asked and
8 answered.
9 A I don't know why you keep using the word
10 "small." I don't know what that means to
11 you.
12 Q Sir, you have your declaration in front
13 of you, right?
14 A Yes.
15 Q Can you turn to Paragraph 50 of your
16 declaration. And I want to turn your
17 attention to where you use the phrasing
18 "small percentage of cancer patients." Just
19 let me know when you have it.
20 A Okay. I have it.
21 Q And you see that you give sworn
22 testimony in your declaration stating:

1 "At the time of the invention of
2 the '393 Patent, it was known that a
3 small percentage of cancer patients,
4 including CRC patients, were MSI-High"?
5 A That's correct.
6 Q And you understood that statement when
7 you wrote it, right?
8 A Correct. I understood that to be on the
9 order of 15 percent.
10 Q Now, it in fact was publicly known by at
11 least 2010 that a small percentage of cancer
12 patients, including colorectal cancer
13 patients, were MSI-High, right?
14 A That's correct.
15 Q And it was also known by 2010 that the
16 tumors of MSI-High cancer patients tended to
17 have high mutational loads and were
18 infiltrated by immune cells, right?
19 A That is correct.
20 Q And that was publicly known by at
21 least 2010, right?
22 A I don't recall the date at which the

1 immune cell infiltration paper came out, but
2 the mutational load was clearly known
3 by 2010.
4 Q Do you recall the publications that you
5 cited in your declaration?
6 A Yes. There is a publication which was
7 from, I think, Walter Bodmer in Nature that
8 discussed the mutational load. But I don't
9 recall the date of the first paper to
10 disclose the lymphocytic infiltration. I
11 just don't recall, sitting here right now.
12 Q Okay. And you realize I didn't ask you
13 if you recall the first paper to discuss
14 that. You realize that, right?
15 A Right. But I just don't -- I don't
16 recall whether or not there was a publication
17 prior to 2010 discussing the lymphocytic
18 infiltration.
19 Q Right. And my question was not about
20 prior to 2010. My question was that it was
21 known at least by 2010 that the tumors of
22 MSI-High cancer patients tended to have

1 higher mutational loads and were infiltrated
2 by immune cells.
3 You would agree with that?
4 A My recollection is clearly that the
5 mutational load was understood, and I don't
6 understand why you are distinguishing prior
7 to 2010 from the wording of your question.
8 Q Okay. Would you agree that prior to the
9 posting of the MSI-High study record it was
10 known that tumors of MSI-High cancer patients
11 tended to have higher mutational loads and
12 were infiltrated by immune cells?
13 A That is correct.
14 Q Now, the POSA, looking at the posted
15 study record, would understand that the trial
16 disclosed in the study record has an
17 anticipated enrollment of 71 patients, right?
18 A I don't have the study records in front
19 of me anymore locally.
20 Q You can bring it up. It's in
21 Exhibit 1005.
22 Your counsel is helping you bring it up.

1 MR. RATLIFF: Thank you, Counsel.
2 A Okay. Could you repeat the question?
3 Q Sure.
4 You would agree that the person of
5 ordinary skill in the art would understand
6 that the trial disclosed in the study record
7 has an anticipated enrollment of 71 patients,
8 right?
9 A I'm just looking for that number.
10 Q Did you look at the study record
11 carefully for this case?
12 A Yes, I did. I'm just looking for the
13 number "71."
14 Q Maybe you can turn your attention to
15 Page 4 of 6 in Exhibit 1005.
16 A I see it. "Enrollment: 71,
17 Anticipated." Yes. That's correct.
18 Q Right. So you would agree that the
19 person of ordinary skill in the art would
20 understand that the trial disclosed in the
21 study record has an anticipated enrollment of
22 71 patients, right?

1 A That's correct.
2 Q And you would agree that the person of
3 ordinary skill in the art would appreciate
4 that the study record identifies eligibility
5 criteria, right?
6 A Yes.
7 Q And would you agree that the person of
8 ordinary skill in the art attempting to
9 conduct a trial disclosed in the study record
10 would see for the inclusion criteria there's
11 ten different things that are listed, right?
12 A Yes.
13 Q Now, I want to talk about those ten
14 different points of inclusion criteria, and
15 starting with the tenth one.
16 So the POSA attempting to conduct a
17 trial disclosed in the study record would
18 understand as part of the inclusion criteria
19 the patient would have to agree to have a
20 biopsy of their cancer, right?
21 A That's correct.
22 Q And you would agree that the POSA

1 attempting to conduct the trial disclosed in
2 the study record would confirm that the
3 patient actually has agreed to have a biopsy
4 of their cancer taken before giving any
5 patient pembrolizumab, right?
6 A No. That's not stated in the study
7 record.
8 Q Okay. So let me just make sure I'm
9 clear on your testimony.
10 You -- I'll ask this way: Would you
11 agree that the person of ordinary skill in
12 the art attempting to conduct the trial
13 disclosed in the study record would confirm
14 that the patient has actually agreed to have
15 a biopsy of their cancer taken --
16 A Yes.
17 Q -- before giving that patient any
18 pembrolizumab?
19 A They would have agreed to have a biopsy
20 of their cancer before being entered into the
21 trial, yes.
22 Q Okay. And would you agree that the

1 person of ordinary skill in the art
2 attempting to conduct the trial disclosed in
3 the study record would have to confirm that
4 the patient was willing and able to comply
5 with study record procedures before giving
6 that patient any pembrolizumab, right?
7 A That's correct.
8 Q And would you agree that the POSA
9 attempting to conduct the trial disclosed in
10 the study record would confirm that the
11 patient has actually signed the informed
12 consent form before giving that patient any
13 pembrolizumab, right?
14 A That's correct.
15 Q And that was including Criteria No. 8,
16 and we'll go to 7, now.
17 Doctor, you would agree that the person
18 of ordinary skill in the art, attempting to
19 conduct a trial disclosed in the study
20 record, would actually confirm that the
21 patient has used an acceptable form of birth
22 control through the study and for 28 days

1 after final dose of the study drug, before
2 giving that patient any pembrolizumab, right?
3 A That's correct.
4 Q And, Doctor, you would agree that the
5 person of ordinary skill in the art
6 attempting to conduct a trial disclosed in
7 the study record, would actually confirm that
8 the patient had adequate organ function as
9 defined by study specified laboratory tests
10 before actually giving any patient
11 pembrolizumab, right?
12 A That's correct.
13 Q And you would agree that the person of
14 ordinary skill in the art attempting to
15 conduct a trial disclosed in the study
16 record, would actually confirm that the
17 patient had a ECOG performance status of zero
18 to one before giving any patient
19 pembrolizumab, right?
20 A That's correct.
21 Q And that was inclusion Criteria No. 5.
22 We'll move on to four.

1 You would agree that the person of
2 ordinary skill in the art attempting to
3 conduct a trial disclosed in the study record
4 would actually confirm that the patient has
5 measurable disease before actually giving any
6 patient pembrolizumab, right?
7 A That's correct.
8 Q Now, looking at inclusion Criteria
9 No. 3, would you agree that the person of
10 ordinary skill in the art attempting to
11 conduct a trial disclosed in the study record
12 would actually confirm that noncolorectal
13 cancer patients are actually MSI positive
14 before giving any noncolorectal cancer
15 patient pembrolizumab, right?
16 A Within the trial, yes, agreed.
17 Q Let me try -- I'm not sure of your
18 response.
19 You would agree that the person of
20 ordinary skill in the art attempting to
21 conduct a trial disclosed in the study
22 record, would confirm for any noncolorectal

1 cancer patients, that that patient actually
2 was MSI-High positive before giving any
3 noncolorectal cancer patients any
4 pembrolizumab, right?
5 A Within the trial, yes, you're right.
6 Q And you would agree that the person of
7 ordinary skill in the art attempting to
8 conduct a trial disclosed in the study
9 record, would confirm that for any colorectal
10 cancer patient, that the colorectal cancer
11 patient is either MSI-High positive or
12 MSI-High negative before giving any
13 pembrolizumab to the patient, right?
14 A I don't think that that requires any
15 determination because any patient is either
16 positive or negative. There's no third
17 alternative.
18 Q So let me try my question again.
19 Would you agree that the person of
20 ordinary skill in the art attempting to
21 conduct a trial disclosed in the study
22 record, would actually confirm for any

1 colorectal cancer patient, whether they're
2 MSI-High positive or MSI-High negative,
3 before giving any colorectal cancer patient
4 pembrolizumab?
5 A You use the word "confirm," there's no
6 need to confirm because there's only two
7 possibilities, they're either positive or
8 negative. So that determination just
9 requires which arm to go into, arm one or arm
10 two.
11 Q Let me try this question.
12 Would you agree that the person of
13 ordinary skill in the art attempting to
14 conduct a trial disclosed in the study
15 record, would actually test any colorectal
16 cancer patient to determine -- or, sorry, let
17 me start this again.
18 Would you agree that the person of
19 ordinary skill in the art attempting to
20 conduct a trial disclosed in the study
21 record, would, for the colorectal cancer
22 patients enrolled in the study, test them to

1 determine whether or not they're MSI-High
2 positive or MSI-High negative before giving
3 them any pembrolizumab?
4 A No.
5 Q Okay. And so, in your view, of the ten
6 inclusion criteria that's listed in the
7 posted study record, the person of ordinary
8 skill in the art attempting to conduct the
9 trial disclosed in the study record would
10 make a confirmation as to inclusion criteria
11 three through ten before giving any patient
12 pembrolizumab, but would not do the same for
13 inclusion criteria one and two; is that fair?
14 A This is a -- this is a biomarker trial
15 that requires a retrospective analysis. And
16 the retrospective analysis is the impact of
17 MSI-High positivity or negativity to the
18 outcome of -- to the therapeutic outcome.
19 Q Let me try my question again because I'm
20 not sure you understood it.
21 You recognize that the person of
22 ordinary skill in the art attempting to

1 conduct the trial disclosed in the study
2 record would see ten inclusion criteria,
3 right?
4 A That's correct.
5 Q And you believe that the person of
6 ordinary skill in the art attempting to
7 conduct the trial disclosed in the study
8 record would actually make a confirmation as
9 to inclusion criteria numbered three, four,
10 five, six, seven, eight, nine and ten, before
11 giving any patient pembrolizumab, but would
12 not do a confirmation as to inclusion
13 criteria one and two?
14 A A person of ordinary skill in the art
15 would be someone who is familiar with
16 designing clinical trials. And this person
17 is going to look at this design. They're
18 going to say, okay, this is a biomarker
19 trial. And there's a couple of reasons to
20 have a sort of a biomarker trial.
21 One is, if you've got a diagnostic that
22 you think is going to be a good diagnostic

1 for selecting patients, but that diagnostic
2 is not yet approved, and so in order to
3 select patients to put them into a particular
4 arm, you would need to get what is called an
5 investigational device exemption from the
6 FDA. And that's a costly process.
7 So, typically, people who have what they
8 think is a good assay, but it's not yet
9 approved, they would design a trial like
10 this. But in this case, the MSI-High
11 diagnostic is out there and is in use, and so
12 if you look at a trial like this, then you're
13 thinking, well, this a trial that's designed
14 to test multiple hypotheses.
15 And, particularly, you look down and
16 see agree to have a biopsy of a cancer. I'm
17 presuming, and I would presume as a person of
18 ordinary skill in the art, that would include
19 something like a PBL1 positivity for the
20 cancer and for the tumor cells. So you're
21 going to be looking at a lot of different
22 biomarkers and determining which single

1 biomarker or set of biomarkers allows you to
2 subset the MSI-High positive colorectal
3 cancer patients from the MSI-High negative
4 colorectal cancer patients in terms of
5 outcome.
6 If, in fact, you were confident that you
7 had a good diagnostic for selecting patient,
8 you would not need arm two at all. Arm two
9 is irrelevant. Arm two is certainly not
10 relevant to regulatory approval and there's
11 no MSI-High negative colorectal cancer subset
12 in the -- in the pivotal trial for this.
13 The -- or required for the pivotal trial for
14 this.
15 And there's also, you know, given that
16 it was known in the art that MSI-High
17 negative colorectal cancer patients, the
18 response rate was exceptionally low, you
19 would be able to recognize a signal without
20 that arm two.
21 But arm two, the inclusion of arm two
22 makes a person of ordinary skill in the art

1 think, well, we don't really know whether or
2 not the MSI-High positivity is going to make
3 a substantial contribution to the patient
4 outcome. And so we're going to look at,
5 potentially a lot of different biomarkers.
6 Q And, Doctor, you would agree that the
7 person of ordinary skill in the art
8 attempting to conduct a trial disclosed in
9 the study record, would know before giving
10 any patient pembrolizumab, that a small
11 percentage of cancer patients were MSI-High?
12 A At the time it would have been assumed
13 to be on the order of 15 percent. And that's
14 going to depend on what pool of patients
15 you're selecting from.
16 Q And you equate 15 percent with being
17 small; is that fair? 15 percent is a small
18 percentage, in your opinion?
19 A It is less than half. But, again, it
20 would depend on what the pool of patients is.
21 I don't know what the pool of patients is.
22 Q Doctor, you remember in your

1 declaration, you say, "At the time of the
2 invention of the '393 Patent it was known
3 that a small percentage of cancer patients
4 were MSI-High," you remember that, right?
5 A Yes. And I was referring to the
6 15 percent number. Which I think -- I don't
7 remember if 15 percent is in my declaration,
8 but certainly in references within -- that
9 were referred to in the declaration.
10 Q So let me ask the question.
11 Would you agree that the person of
12 ordinary skill in the art attempting to
13 conduct the trial disclosed in the study
14 record, before they give any patient
15 pembrolizumab would understand that only a
16 small percentage of cancer patients,
17 including colorectal cancer patients, were
18 MSI-High?
19 MR. MILLER: Objection, form.
20 Go ahead.
21 A I don't know what pool of patients
22 they're selecting from.

1 MR. MILLER: Preston, we've been going
2 for well over an hour. Is this a good
3 time?
4 MR. RATLIFF: Dr. Lonberg, would you
5 like to take a break?
6 THE WITNESS: Yes, please. Thank you.
7 (Whereupon, a recess was taken
8 from 2:39 PM until 2:51 PM.)
9 Q Doctor, during the break, did you
10 discuss any of your testimony?
11 A No.
12 Q During the break, did you discuss this
13 case?
14 A No.
15 Q Doctor, do you believe that the trial
16 disclosed in the MSI-High study record was a
17 retrospective clinical study?
18 A Yes.
19 Q And you have read the package insert for
20 KEYTRUDA, correct?
21 A Yes.
22 Q And do you know whether or not the

1 package insert for KEYTRUDA, if it describes
2 the clinical trial disclosed in the MSI-High
3 study record as a retrospective versus a
4 prospective clinical study?
5 A I don't -- I don't recall.
6 Q You don't recall either way?
7 A No.
8 Q But when you read the package insert
9 that you actually cite in your declaration,
10 you read that carefully, right?
11 A Yes.
12 Q You weren't confused by anything in the
13 package insert when you read it, right?
14 A No.
15 Q And you don't distrust anything that was
16 written in the package insert, do you?
17 A No.
18 Q Do you believe that the person of
19 ordinary skill in the art -- strike that.
20 Doctor, I want to turn your attention
21 back to the '393 Patent. And in particular,
22 we had a discussion earlier regarding

1 Claims 31, 33, 35, 37, 39 and 41.
2 So my question to you, Doctor, is, as
3 you understand it, each of those Claims 31,
4 33, 35, 37, 39, and 41 of the '393 Patent,
5 they require a statistical determination
6 step; is that fair?
7 MR. MILLER: Objection, form.
8 A They require a determination step and
9 the validity -- well, whether or not the
10 claims are relevant requires a determination
11 step, and the significance of that
12 determination step requires a statistical
13 analysis.
14 Q Is a determination step that you're
15 referring to, is that a mathematical
16 calculation?
17 A No. The determination step is -- well,
18 it includes simple math, but it is the
19 radiologic assay for looking at shrinkage or
20 growth of the tumors.
21 Q Okay. Do the claims that we're
22 referring to, do they have any different

1 clinical treatment steps other than the
2 clinical treatment steps that we talked about
3 in Claim 1 and Claim 14 of the '393 Patent?
4 A No.
5 Q So those Claims 31, 33, 35, 37, 38 and
6 41, in terms of a clinical treatment step,
7 just have the same two clinical treatment
8 steps that we discussed in Claims 1 and 14 of
9 the '393 Patent, right?
10 A Correct. That's two steps, yes.
11 Q Now, the posted study record, and this
12 is Exhibit 1005, it does not identify the
13 trial disclosed in it as an all comers trial,
14 right?
15 A The words "all comers" don't show up in
16 the study record.
17 Q Right. And the person of ordinary
18 skill, looking at the posted study record,
19 would see that it has only three experimental
20 arms, right?
21 A That is true.
22 Q And the person of ordinary skill would

1 understand that the posted study record
2 provides that there will be both colorectal
3 cancer patients, as well as noncolorectal
4 cancer patients in the study, right?
5 A That is correct.
6 Q And the person of ordinary skill in the
7 art would understand that the trial disclosed
8 in the posted study record does not permit
9 enrollment of patients that are MSI-High
10 negative and had noncolorectal cancer, right?
11 A They would not be included in the trial.
12 Q Okay. And I want to be sure I got an
13 answer to my question about the person of
14 ordinary skill in the art.
15 Would you agree that the person of
16 ordinary skill in the art would understand
17 that the trial disclosed in the posted study
18 record provides that there will be both
19 colorectal cancer patients as well as
20 noncolorectal cancer patients?
21 MR. MILLER: Objection, form.
22 A That's correct.

1 Q Okay. And you would agree that the
2 person of ordinary skill in the art would
3 understand that the trial disclosed in the
4 posted study record does not permit
5 enrollment of patients that are MSI-High
6 negative and have noncolorectal cancer,
7 right?
8 A That's correct.
9 Q And based on an objective read of the
10 posted study records, you would agree that
11 the person of ordinary skill in the art would
12 understand that all noncolorectal cancer
13 patients would need to be tested and
14 determined their MSI-High status before
15 giving them Pembrolizumab, right?
16 A Within the trial, correct.
17 Q And you would agree that the person of
18 ordinary skill in the art would understand
19 that the trial does not involve noncolorectal
20 MSI stable patients, right?
21 A That's correct.
22 Q You would agree the person of ordinary

1 skill in the art would understand that the
2 posted study record has a parallel assignment
3 interventional study record, right?
4 A Can you say that again?
5 Q You would agree that the person of
6 ordinary skill in the art would understand
7 that the posted study record has a parallel
8 assignment interventional study model, right?
9 A Yes. It's multiple arms with the same
10 intervention.
11 Q By parallel that means the treatment for
12 each of the three arms are given about the
13 same time, right?
14 MR. MILLER: Objection. Form.
15 A I don't know what the -- how the actual
16 enrollment unfolded, so I can't say that.
17 Q I'm asking about the meaning of parallel
18 assignments.
19 You see parallel assignment in the study
20 record, right?
21 A Yeah, it means it can happen, but I
22 don't know what actually happened. I don't

1 know whether they filled up --
2 Q Okay. And I'm not asking about what
3 actually happened. I'm asking you about your
4 understanding of the term parallel assignment
5 when it comes to an interventional study
6 model.
7 So here's my question: A parallel
8 assignment means that the treatment for each
9 of the arms in the study are given about the
10 same time, right?
11 MR. MILLER: Objection. Form.
12 A It means that they can be, but it
13 depends, the actual timing of treatment
14 depends on whether or not, on which arm gets
15 enrolled first and which arm fills up first.
16 So it's -- it doesn't -- parallel assignment
17 doesn't imply parallel therapy.
18 Q Okay. So parallel assignment confers to
19 you what then?
20 A It means that you are not first filling
21 up arm one and then recruiting patients for
22 arm two and then recruiting patients for arm

1 three. There's no -- that you are assigning
2 patients for all three arms as patients come
3 in.
4 Q Okay. And is it your belief that the
5 POSA attempting to conduct the clinical trial
6 disclosed in the study record, knowing that
7 they would need to test noncolorectal cancer
8 patients to determine their MSI-High status,
9 would not at the same time attempt to test
10 the colorectal cancer patients that are in
11 arms one and two of the study?
12 A I don't think there's a requirement to
13 report to conduct the study given that you've
14 got two different arms, negative and
15 positive.
16 Q I didn't ask if there was a requirement.
17 A I don't even think there's a practical
18 requirement for it.
19 Q You understand that I didn't ask if
20 there was a practical requirement, right?
21 A Now, you're asking that, no.
22 Q Would you agree that the POSA attempting

1 to conduct the clinical trial that's
2 disclosed in the study record, knowing that
3 they would need to test noncolorectal cancer
4 patients to determine their MSI-High status,
5 would also attempt about the same time to
6 test the colorectal cancer patients in arms
7 one and two to determine their MSI-High
8 status, right?
9 MR. MILLER: Objection. Form.
10 A No.
11 Q Okay. Now, you read the board's
12 institution decision, right?
13 A I don't recall.
14 Q You don't recall reading the board's
15 institution decision?
16 A I don't recall.
17 Q Do you know what I mean by the board's
18 institution decision?
19 A Yes.
20 Q Let's take a look at your declaration
21 and if you could turn to Paragraph 96 and let
22 me know if you have it, should be Page 53 of

1 your October 4, 2024 declaration.
2 A Yes.
3 Q So you see in Paragraph 96, you
4 reference the board and the board's
5 institution decision?
6 A Yes.
7 Q Sitting here today, is it correct that
8 you read the institution decision?
9 A Yes.
10 Q And did you read it carefully?
11 A Yes.
12 Q And when you read it, did you understand
13 it?
14 A Yes.
15 Q Now, in your opinions, the plain and
16 ordinary meaning of the claim language in
17 response to as used in the claims of '393
18 Patent requires a causal relationship, right?
19 A Yes.
20 Q And that causal relationship is between
21 determining that a patient's colorectal
22 cancer is Microsatellite Instability-High or

1 DNA mismatch repair deficient and treating
2 the patient with pembrolizumab, right?
3 A Depending on the outcome.
4 Q Let me try that again.
5 In your opinion, the plain and ordinary
6 meaning of the term in response to requires a
7 causal relationship between one, determining
8 that a patient's colorectal cancer is
9 Microsatellite Instability-High or DNA
10 mismatch repair deficient; and two, treating
11 the patient with pembrolizumab, right?
12 A Right, but it's in response to the
13 outcome of that test.
14 Q Now, Dr. Lonberg, do you recall giving
15 sworn testimony in your declaration to the
16 effect that in your opinions the plain and
17 ordinary meaning of the term "in response to"
18 requires a causal connection -- a causal
19 relationship, sorry, between one, determining
20 that a patient's colorectal cancer is
21 Microsatellite Instability-High or DNA
22 mismatch repair deficient; and two, treating

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

1 June 13, 2024, and we should be able to put
2 that in the chat so you can take a look at
3 it.
4 (Whereupon, Decision Granting
5 Institution of Inter Partes
6 Review, dated 6-13-24 was marked
7 as Exhibit Paper 10 for
8 identification as of this date.)
9 TECH WELCH: I apologize counsel,
10 which exhibit is that?
11 MR. RATLIFF: It's called paper No. 10
12 it's not an actual exhibit.
13 TECH WELCH: Understood.
14 MR. RATLIFF: Let me know if you're
15 not able to find it.
16 TECH WELCH: I see it. Should be
17 uploading one moment.
18 MR. RATLIFF: Thank you so much.
19 Q Dr. Lonberg, let me know when you have
20 the board's institution decision that you
21 said you read very carefully and that you
22 understood.

1 A Okay, I have it.
2 Q Now, if I could turn your attention to
3 Page 16 of the institution decision.
4 Are you there?
5 A Yes. I'm on Page 16.
6 Q Okay. And if I could turn your
7 attention to it's near the top of the page of
8 16 where there's a sentence that begins
9 "petitioner has sufficiently shown."
10 Do you see that?
11 A Yes.
12 Q And do you see that it reads,
13 "Petitioner has sufficiently shown that there
14 is a reasonable likelihood of a causal
15 relationship in the MSI-High study record
16 between treatment of colorectal cancer
17 patients and the determination of their
18 MSI-High status."
19 Do you see that?
20 A Yes.
21 Q And that was a statement that the board
22 made, right?

1 A Yes.
2 Q So you understand that the board did not
3 ignore the claim language in response to --
4 strike that.
5 You understand that the board did not
6 ignore that the claim language in response to
7 found in the claims of the '393 Patent
8 involved a causal relationship between
9 treatment of colorectal cancer patients and
10 determination of their MSI-High status,
11 right?
12 MR. MILLER: Objection. Form.
13 A That seems to be the implication because
14 they do bring up causal relationship.
15 Q Now, you prepared two declarations for
16 this matter, right?
17 A That's correct.
18 Q And there was a March 14, 2024,
19 declaration that you prepared, right?
20 A That's correct.
21 Q We have been discussing today an October
22 4, 2024, declaration that you prepared,

1 right?
2 A Correct.
3 Q Just to be clear, you read those
4 declarations carefully before you signed
5 them, right?
6 A Excuse me, could you repeat the
7 question.
8 Q Sure. Just to be clear, you read those
9 declarations, your March 14, 2024, and your
10 October 4, 2024, declarations carefully
11 before you signed them, right?
12 A That's correct.
13 Q And did you understand every statement
14 you made in those declarations before you
15 signed them?
16 A Yes, I did.
17 Q And sitting here today, do you believe
18 that there are any errors in your
19 declaration?
20 A No.
21 Q And sitting here today, are they
22 corrections that you would like to make with

1 respect to either of your declarations?
2 A I can't think of any.
3 Q Now, as far as your work in this case,
4 you had a meeting with Dr. Goldberg, right?
5 A That's correct.
6 Q And that's Dr. Richard Goldberg, one of
7 the declarants for JHU, in this case, right?
8 A He's a declarant, I don't recall his
9 first name.
10 Q Was your meeting with Dr. Goldberg in
11 person?
12 A No.
13 Q How did it occur, was it by phone?
14 A It was a Zoom call.
15 Q Zoom call.
16 And how long was your meeting with
17 Dr. Goldberg?
18 A It was relatively short. I don't
19 remember the exact time, on the order of
20 30 minutes. Could have been longer.
21 Q You said relatively short, so how much
22 beyond 30 minutes in your view is relatively

1 short?
2 A It would have been an hour or less but
3 my recollection was that it was less than an
4 hour, that's my recollection.
5 Q Okay. And other than yourself and
6 Dr. Goldberg, did anyone else attend this
7 meeting?
8 A Yes.
9 Q Who attended the meeting?
10 A Attorneys for Hopkins.
11 Q Anyone else attend the meeting?
12 A No.
13 Q And what did you discuss with
14 Dr. Goldberg during this meeting?
15 A It's the first time that I had ever met
16 him so there was a little bit of meet and
17 greet and then we discussed some aspects of
18 his declaration, including his analysis of
19 the relevance of the claims with respect to
20 practicing the therapies that are described
21 in the packages for pembrolizumab.
22 Q And you said you reviewed his

1 declaration, so when did this meeting occur?
2 A I don't recall the exact time, it was
3 several months ago I think. I was in
4 Michigan at the time so I should be able to
5 figure that out.
6 Q Did this meeting occur before or after
7 you signed your declaration?
8 A I don't recall.
9 Q And you said you talked about his
10 declaration, did you have a copy of
11 Dr. Goldberg's declaration at the time of
12 this meeting?
13 A I don't recall.
14 Q How did you talk about the declaration?
15 A We talked specifically about the
16 relevance of the claims in the '393 Patent to
17 therapies described in the package insert for
18 pembrolizumab.
19 Q Right. And you say at the time of the
20 meeting you were in the Michigan, so how
21 would you determine when the meeting actually
22 occurred?

1 A The fastest way would be to look on my
2 phone and look in my photos and look for
3 photos from Holland, Michigan.
4 Q Do you have your phone nearby that you
5 can do that?
6 A Yes. I can do that.
7 Q That would be great if you can please
8 review your phone and let me know when you
9 believe this meeting occurred with
10 Dr. Goldberg?
11 A It would have been the first week of
12 October from my memory.
13 Q Do you have a better date than that, the
14 first week of October?
15 A We arrived in Michigan on October 3rd,
16 so it would have been after October 3rd.
17 Q Do you know if it was October 4th, or
18 5th or beyond?
19 A No. I don't recall.
20 Q And you say when you met with
21 Dr. Goldberg you say that you reviewed his
22 declaration, right?

1 A I don't recall. We discussed the
2 declaration. I don't recall the order in
3 which I reviewed the declaration and the --
4 or which parts of the declaration and the
5 phone call or the Zoom call, no, I don't.
6 Q Well, when you said that you reviewed
7 his declaration, did you review it in its
8 entirety or did you only look at parts?
9 A I don't recall.
10 Q Did you review the declarations of any
11 other JHU declarants?
12 A I'm trying to recall. I believe that I
13 reviewed the declarations of Dr. Pardoll and
14 Dr. Le, and I -- there may have been others.
15 I'm just -- don't recall right now offhand.
16 Q Okay. But you're confident that you
17 reviewed the declarations by Dr. Pardoll and
18 is Dr. Le, right?
19 A That is correct.
20 Q And was there just one meeting with
21 Dr. Goldberg or were there multiple meetings
22 that you had?

1 A Just that one meeting.
2 Q Okay. So in this case did you ever
3 speak with Jennifer Newberger?
4 A Jennifer Newberger, no.
5 Q And you did not ever speak with Brian
6 Segers, right?
7 A No.
8 Q As part as your work in this matter, did
9 you have any meetings or discussions with any
10 other JHU consultants or experts?
11 A No. I have only spoken to the JHU
12 attorneys from Fish & Richardson about this
13 case.
14 Q And as part of your work in this case,
15 you didn't speak with Dr. Le, right?
16 A No. I haven't spoken to --
17 Q As part of your work --
18 A I haven't spoken to Dr. Le in over
19 ten years.
20 Q And as part of your work in this matter,
21 you didn't ever speak with anyone employed by
22 JHU, right?

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

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

1 deposition was anything related to this case?
2 Is that your testimony?
3 MR. MILLER: Objection to form.
4 Go ahead.
5 A I do not believe so.
6 Q Okay. Did you speak with any in-house
7 counsel at Bristol Myers as part of your work
8 in this case?
9 A No.
10 Q Now, do you still have a copy of the
11 posted study record, Exhibit 1005?
12 A Yes.
13 Q Okay. And would you agree that at the
14 time of the posting of the study record,
15 MSI-High testing was already standardized and
16 performed in CLIA-certified laboratories
17 without the need for assay development?
18 A That's correct, and that's why the
19 design of this trial, to a person of ordinary
20 skill in the art, would have looked like a
21 biomarker trial in retrospective analysis.
22 Because otherwise, there would have been no

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

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

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

1 questions, and you can provide responses. So
2 let me try this again.
3 Do you think that it would have been
4 unreasonable at the time of the study
5 record's posting to reasonably anticipate an
6 outcome that there would be a greater number
7 of clinical responses in the MSI patient
8 group than the MSS group?
9 MR. MILLER: Objection. Form. Asked
10 and answered.
11 A I think it would unreasonable to
12 anticipate a particular outcome. That's not
13 why you do a clinical trial. You do a
14 clinical trial to test a hypothesis. You
15 don't anticipate a particular outcome.
16 If you anticipated a particular outcome
17 and you wanted to just see whether or not the
18 number of responses was high enough to get a
19 particular approval with a particular number
20 of patients in a pivotal trial, you would not
21 have done Arm 2. There's no reason to do
22 Arm 2 if you had anticipated an answer.

1 Q Would you agree that at the time of the
2 study record's posting on clinicaltrials.gov
3 part of the rationale for doing such a study
4 was that BMS's PD-1-blocking antibody
5 nivolumab showed activity in melanoma?
6 MR. MILLER: Objection. Form.
7 A It was known that nivolumab and
8 pembrolizumab were active drugs, and that is
9 an obvious motivation for doing exploratory
10 trial in different subsets of patients,
11 different populations of patients.
12 Q Okay. I just want to be sure we're
13 clear, would you agree that at the time of
14 the MSI-High study record's posting on
15 clinicaltrials.gov, part of the rationale for
16 doing such a study was that BMS's
17 PD-1-blocking antibody nivolumab showed
18 activity in melanoma?
19 MR. MILLER: Objection. Form.
20 A It showed activity in melanoma and in
21 other cancer types.
22 Q Okay. And I just want to -- I'm asking

1 a question about the rationale, so let me try
2 it again, make sure we're on the same page.
3 Would you agree that at the time of the
4 study record's posting part of the rationale
5 for doing such a study was that BMS's
6 PD-1-blocking antibody nivolumab showed
7 activity in melanoma?
8 MR. MILLER: Objection. Form. Asked
9 and answered.
10 A Part, yes. You used the word "part" in
11 your question. Because it was also known to
12 be active in other cancer types.
13 Q Understood. And so you would agree that
14 at the time of the study record's posting
15 part of the rationale for doing such a study
16 was that BMS's PD-1-blocking antibody
17 nivolumab showed activity in non-small cell
18 lung cancer, right?
19 A Correct.
20 Q And you would agree that at the time of
21 the MSI-High study record's posting part of
22 the rationale for doing such a study was that

1 BMS's PD-1-blocking antibody nivolumab had a
2 complete response in a single patient with
3 colorectal cancer, right?
4 A That's correct.
5 Q And that complete response in that
6 single patient was a MSI-High colorectal
7 cancer patient, right?
8 A I don't know when that became public.
9 And so when that would have been accessible
10 to a person of skill in the art, but yes, it
11 turned out that that person was MSI-High.
12 Q Okay. And you would agree that
13 pembrolizumab and nivolumab have the same
14 mechanism, right?
15 A That's correct.
16 Q And a POSA would have known that at the
17 time of the study record's posting on
18 clinicaltrials.gov, right?
19 A That's correct.
20 Q And you would agree that at the time of
21 the study record's posting preclinical
22 studies suggested that pembrolizumab and

1 nivolumab have a similar potency, right?
2 A That's correct.
3 Q And the person of ordinary skill in the
4 art would have known that at the time of the
5 study record's posting on clinicaltrials.gov,
6 right?
7 A That is correct.
8 Q And you would agree that at the time of
9 the study record's posting PK, or
10 pharmacokinetic modeling suggested that
11 pembrolizumab and nivolumab have similar
12 pharmacokinetics, right?
13 A That's correct.
14 Q And the POSA would have known that at
15 the time of the study record's posting,
16 right?
17 A That is correct.
18 Q Now, would you agree with me that by the
19 time of the critical date, there were
20 publications discussing the clinical
21 relevance of microsatellite instability in
22 colorectal cancer, right?

1 A I'm sorry. Can you refer me to a
2 particular paper?
3 Q I'm not asking about a particular paper
4 right now.
5 My question is would you agree with me
6 that by the time of the critical date,
7 July 10, 2015, there were publications
8 discussing the clinical relevance of
9 microsatellite instability in colorectal
10 cancer patients?
11 A That's correct, yes.
12 Q As part of your work on this case, you
13 read a 2010 article by Chapelle, right?
14 A It sounds familiar. Can I look at my
15 declaration to look at it? Do you remember
16 what the exhibit number was?
17 Q The exhibit number is 1007.
18 (Whereupon, "Clinical Relevance
19 of Microsatellite Instability in
20 Colorectal Cancer," published
21 7-10-10 was marked as Exhibit
22 1007 for identification as of

1 this date.)
2 Q And we can put that in the chat so you
3 can take a look at it if it helps.
4 A Yes. I read Chapelle.
5 Q Okay. And when you read Chapelle, you
6 read it objectively, right?
7 A That's correct.
8 Q You didn't add any bias to your read of
9 Chapelle, right?
10 A No.
11 Q And you read it from the perspective of
12 how the person of ordinary skill in the art
13 would read it, right?
14 A That's correct.
15 Q And you would agree with Chapelle -- let
16 me start that again.
17 You would agree with the Chapelle
18 group's assessment that by the publication
19 date of their article it had been relatively
20 well established that the prognosis is better
21 for patients with MSI-High colorectal
22 cancers, right?

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

1 critical date when my question dealt with the
2 publication date of the Chapelle group's
3 article, and that was in 2010. So let me try
4 my question again.
5 Would you agree with me -- or strike
6 that.
7 Would you agree with the Chapelle
8 group's assessment that by the publication
9 date of their article, it had been relatively
10 well established that the prognosis is better
11 for patients with MSI-High colorectal cancer?
12 A I would have to go back and review the
13 literature specifically to understand that
14 publication date, what the understanding was
15 at that publication date.
16 Q Okay. Well, you would agree that the
17 POSA reading Chapelle would understand that
18 the Chapelle group believed at the time of
19 their publication it had been relatively well
20 established that the prognosis is better for
21 patients with MSI-High colorectal cancer,
22 right?

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

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

1 it's independent of therapy, of standard
2 therapy, because there's a complication of
3 what is the prognosis given standard therapy.
4 And so I think it's a little bit
5 complicated. They're referring here to what
6 I was referring to, which is that it wasn't a
7 completely settled field at the time because
8 they're referring to lack of control group in
9 a particular paper, things like that. And
10 then there was quite a bit of preclinical
11 data on the affect of MSI-High on the
12 sensitivity of the cancer cells themselves to
13 find a few. So I think it was a little bit
14 of a complicated area at the time.
15 Q Okay. Let me ask my question again.
16 Would you agree that the person of
17 ordinary skill in the art reading the
18 Chapelle paper would understand that the
19 Chapelle Group believed in 2010 that it had
20 been relatively well established that the
21 prognosis is better for patients with
22 MSI-High colorectal cancer as they write in

1 their paper?
2 MR. MILLER: Objection. Asked and
3 answered.
4 A Yeah. But it's part of a longer
5 sentence where they're sort throwing that
6 out, and then they're saying, but it's a
7 little more complicated because they're
8 talking about prognosis, an underlying
9 prognosis in the absence of therapy. Then
10 they bring up the complication of outcome for
11 chemotherapy.
12 Q Well, the remainder of the sentence
13 reads whether or not MSI status predicts
14 response to adjuvant chemotherapy has been
15 more controversial, right?
16 A Exactly. That's going to be layered on
17 to an actual prognosis if you've got a
18 population of patients that has been treated
19 with adjuvant chemotherapy. And so I --
20 Q And Dr. --
21 A Sorry. I think --
22 Q I'm only asking --

1 MR. MILLER: Preston, you're
2 interrupting him. Let him finish his
3 answer before you ask your next
4 question.
5 MR. RATLIFF: But I don't think you
6 understand my question.
7 MR. MILLER: It doesn't matter. Let
8 him answer, then you can ask another
9 question or clarify.
10 A I think Chapelle is recognizing how
11 complicated this area is.
12 Q Let's go back to my question.
13 Do you see that the remaining part of
14 the sentence states whether or not MSI status
15 predicts response to adjuvant chemotherapy
16 has been more controversial.
17 Do you see that?
18 A Yes.
19 Q And you would agree that the person of
20 ordinary skill in the art would see that,
21 right?
22 A Yes.

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

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

1 look at the size, using gel electrophoresis.
2 Then a much easier to assay to perform
3 with the immunohistochemistry assay which
4 looked at specific enzymes associated with
5 DNA mismatch repair. And then the subsequent
6 innovation of direct DNA sequencing of the
7 tumor.
8 Q And the POSA would know that by the time
9 of the July 10, 2015 critical date, right?
10 A That's correct.
11 Q Now, as part of your work on this case,
12 you read a 2014 publication by Salipante,
13 right?
14 A That sounds familiar.
15 Q And that publication was all about
16 microsatellite instability detection by next
17 generation sequencing, right?
18 A I'd have to look at it, but that sounds
19 familiar.
20 Q Okay. And do you remember, when you
21 read Salipante, did you read it objectively?
22 A Yes.

1 Q You didn't have any bias to your read of
2 Salipante, right?
3 A No.
4 Q And would you agree that the person of
5 ordinary skill in the art would understand
6 that Salipante's group had an assessment at
7 the time of their publication that it had
8 been established that MSI-High is a useful
9 phenotype in cancer diagnosis and prognosis,
10 right?
11 A That is my recollection. But, again, I
12 don't have the paper in front of me.
13 Q Okay. And would you agree that the POSA
14 would understand from Salipante Group, that
15 by the time of their publication, diagnosis
16 of MSI often had important clinical
17 implication, including informing therapeutic
18 choices, cancer prognosis and familiar cancer
19 risk, right?
20 A I think the latter two are well
21 established, and the therapeutic choices was
22 less well established.

1 Q But the POSA would understand that with
2 the assessment of the Salipante Group, right?
3 A I'd have to go back and look at the
4 Salipante paper.
5 Q We can take a look at the paper. Let's
6 bring up Exhibit 1010.
7 (Whereupon, "Microsatellite
8 Instability Detection by Next
9 Generation Sequencing,"
10 published September 2014 was
11 marked as Exhibit 1010 for
12 identification as of this date.)
13 Q You can let me know when you have it.
14 A Okay. I have the paper.
15 Q Do you recall reading this paper as part
16 of your work on this case?
17 A Yes.
18 Q And can you turn your attention to
19 Exhibit No. 4, Exhibit page number four, it
20 should be at the bottom of the document.
21 A Yes.
22 Q And do you see where the writers of this

1 publication begin to write:
2 "Diagnosis of MSI-High often has
3 important clinical implications"?
4 A Where is that on the page? I see it.
5 Okay. So they have references five
6 through seven. So I'd have to go and look
7 at -- I'd have to go and look at references
8 five through seven to see whether or not I
9 would agree with that. I've lost the --
10 Yeah. I'd have to go back and look at
11 those references.
12 Q Okay. I don't think you understand my
13 question.
14 So my question is not whether or not --
15 let me just try my question.
16 Would you agree that the person of
17 ordinary skill in the art, looking at the
18 Salipante Group papers, would understand that
19 the Salipante Group had stated publicly,
20 diagnosis of MSI often has important clinical
21 implications in forming therapeutic choices,
22 cancer prognosis and familiar cancer risk

1 appraisal?
2 A Well, the authors of this paper are
3 experts at developing diagnostics. And so
4 I'm not sure that a person skilled in the art
5 would take it face value a conclusion like
6 that.
7 Q So, in your view, the person of ordinary
8 skill in the art would do an assessment of
9 who are the writers of the publication --
10 A No.
11 Q -- and come to a -- I wasn't finished
12 with my question.
13 Is it your testimony that the person of
14 ordinary skill in the art, reviewing the
15 prior art, would do an assessment of the
16 writers of the prior art and make a
17 determination whether or not they are
18 qualified to make the statements that they
19 make in those pieces of prior art?
20 A Is that it?
21 MR. MILLER: Objection, form.
22 Q Yes. Is that a step you believe that

1 the person of ordinary skill in the art would
2 take?
3 MR. MILLER: Objection, form.
4 A I believe that a person of ordinary
5 skill in the art would not take that
6 statement at face value. And that they would
7 understand that there's a little bit of
8 promotion, it goes on in that paper,
9 particularly a paper about a new diagnostic.
10 So that sentence looks a little bit
11 promotional.
12 So, anyway, they would read carefully
13 references five through seven, reference one,
14 reference two, reference eight through ten.
15 Q So I understand you have positions,
16 Doctor, but my question was different. It
17 actually wasn't about this particular paper.
18 It was broader. So let me go back to my
19 question.
20 Do you believe that the person of
21 ordinary skill in the art would take the step
22 for any prior art reference they read of

1 making a determination of whether or not the
2 writers of that prior art had the necessary
3 background to make the statement in the prior
4 art that's before the POSA?
5 MR. MILLER: Objection, form.
6 Q Is that a step that you think the POSA
7 can make?
8 A There is this sort of invocation of
9 authority that you see sometimes in the
10 scientific community. And it is an incorrect
11 attitude. I don't remember the Latin phrase
12 that is the motto of the British scientific
13 society, but it pokes fun at that.
14 I don't think that a good scientist, and
15 certainly not a person of skill in the art,
16 would believe that the invocation of
17 authority. I think you roll down and you
18 look at the data. And so that's why you read
19 papers five through seven, paper one, paper
20 two, and papers eight through ten. You don't
21 just rely on invocation of authority.
22 Q Okay. But would you agree that the

1 person of ordinary skill in the art, looking
2 at the Salipante Group's paper, would believe
3 that the Salipante Group is of the opinion
4 that diagnosis of MSI often has important
5 clinical implications in forming therapeutic
6 choices, cancer prognosis and familial cancer
7 risk appraisal?
8 MR. MILLER: Objection, form.
9 A A person of skill in the art would have
10 thought that that was irrelevant what the
11 Salipante Group thought.
12 Q But I'm not asking if they -- what the
13 person of ordinary skill in the art would
14 have thought was relevant or irrelevant. I'm
15 asking you a different question.
16 Do you believe that the person of skill
17 in the art, looking at the Salipante paper,
18 would believe that the Salipante Group were
19 of the opinion that diagnosis of MSI often
20 has important clinical implications,
21 informing therapeutic choices, cancer
22 prognosis and familiar cancer risk appraisal?

1 MR. MILLER: Objection, form.
2 A I don't think that's a determination
3 that requires a person of ordinary skill in
4 the art. I think even a lawyer could read
5 that and say that's the plain English in this
6 piece of paper.
7 Q And do you understand that the Salipante
8 paper explains that evaluation of the MSI
9 phenotype by next-generation sequencing is
10 valuable?
11 A I'm sorry. Could you repeat the
12 question.
13 Q Do you understand that Salipante
14 explains that evaluating MSI phenotypes by
15 next-generation sequencing is valuable?
16 A Yes. That's what is stated in the
17 paper, and it's also what I think a person of
18 ordinary skill in the art would have thought.
19 MR. MILLER: Preston, are you close to
20 closing out on this referent?
21 MR. RATLIFF: I am not.
22 MR. MILLER: All right. We've been

1 going well over an hour, and we're
2 getting to lunchtime here. We would
3 like to take a break.
4 MR. RATLIFF: Dr. Lonberg, would you
5 like to break for lunch?
6 THE WITNESS: Yes --
7 MR. RATLIFF: Or just take a break?
8 THE WITNESS: Yes, please. Take a
9 break for lunch.
10 MR. RATLIFF: Okay. It's almost
11 1:00 p.m. Pacific?
12 MR. MILLER: Correct.
13 MR. RATLIFF: How does half an hour
14 sound or 45 minutes? What works for
15 you, Doctor?
16 MR. MILLER: Somewhere between 30 and
17 45.
18 MR. RATLIFF: Okay. Sounds good.
19 (Whereupon, a recess was taken
20 from 3:59 PM until 4:41 PM.)
21 Q Doctor, do you have a copy of the
22 '393 Patent in front of you?

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

1 referring to. Was it Pernot? Is that the
2 paper you're referring to?
3 Q I'm not referring to any particular
4 paper. I'm asking you would you agree that
5 before the critical date that there were
6 publications stating that colorectal cancer
7 associated MSI could lead to a more intense
8 immune response, making such patients good
9 candidates for immunotherapy?
10 A Yeah, I believe -- well, Pernot is prior
11 to the critical date. I believe Pernot has
12 language like that.
13 Can I pull Pernot up? Can we pull it up
14 so that I can point you to the language that
15 I think you're referring to?
16 Q Sure. Let's take a look at -- I believe
17 Pernot is Exhibit 1006.
18 (Whereupon, "Colorectal cancer
19 and immunity," published 4-14-14
20 was marked as Exhibit 1006 for
21 identification as of this date.)
22 TECH WELCH: 1006 is uploading now.

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

1 main point of this paper because they're
2 talking about -- you'll see that leading up
3 to that sentence, the "altogether" sentence,
4 is a discussion of specific mechanisms by
5 which MSI-High tumors evade the immune
6 system.
7 And there's two particular mechanisms
8 they call out. One is the high density of
9 intratumoral regulatory T cells, and the
10 other is the lower expression of HLA.
11 And so then what that sentence
12 "altogether" is referring to is that when
13 they say "specific immunoregulatory
14 phenomenon" is that if you had drugs that
15 could target the specific immune evasion
16 mechanisms, that would be an interesting path
17 for immunotherapy.
18 And so if you had, for example, a drug
19 like ipilimumab that depletes regulatory T
20 cells or perhaps a cytokine therapy that
21 induces HLA class II -- although they don't
22 discuss HLA class II, which could compensate

1 for lower HLA class I. That if you had drugs
2 like that, that might be interesting because
3 you've already got a tumor that is selected
4 for dependence on those particular
5 mechanisms.
6 PD-1 blockade is not a mechanism like
7 that, so I don't read this as having anything
8 to do with PD-1 blockade.
9 Q Do you know what was my question that I
10 asked you?
11 A If you want to repeat your question,
12 that would be great.
13 Q Now, I'm just asking do you know what my
14 question was. I don't want to repeat it. Of
15 course I don't want to waste time to repeat
16 it.
17 Do you know what I asked you?
18 A I would like you to repeat it.
19 Q It's not helpful for me to repeat. I
20 just want to make sure -- I'm trying to be
21 mindful of your time, and if we're not
22 understanding the questions, then I'm just

1 trying to make sure we appreciate that. But
2 let me try my question again.
3 Do you agree that before the critical
4 date, July 10, 2015, there were publications
5 stating that colorectal cancer associated
6 with MSI could lead to a more intense immune
7 response, making such patients good
8 candidates for immunotherapy?
9 A That's almost exactly what's written
10 right on Page 5 in the sentence that you
11 directed me to. But I don't think that
12 immunotherapy in this case is referring to
13 PD-1 blockade.
14 Q Okay. And would you agree that the POSA
15 would have seen in the Pernot article -- and
16 this is Exhibit 1006 -- specific mention of
17 molecules called "immune checkpoints"?
18 A Yeah. That was mentioned almost in
19 passing. Let me see if I can pull that up.
20 Under other escape mechanisms are suspected
21 in CRC, B7H1 or PDL-1 --
22 MR. MILLER: You're going to have to

1 go slower if you're going to read.
2 THE WITNESS: Oh. Sorry.
3 A So this is on Page 3742:
4 "Recently some monoclonal
5 antibodies targeting these molecules
6 (PD1, CTLA-4) have shown more than
7 promising efficacy results in solid
8 neoplasia such as melanoma and others."
9 Q Okay. Are you ready to answer my
10 question?
11 A Do you want to repeat your question?
12 Q Sure.
13 Would you agree that the POSA looking at
14 the Pernot article would have seen a specific
15 mention of molecules called "immune
16 checkpoints"?
17 A I don't doubt that is in here but -- oh,
18 there it is. Yes. I agree, yes.
19 Q Okay. And you would have seen -- would
20 you agree that the POSA would have seen that
21 the Pernot article specifically references
22 the immune checkpoint inhibitors ipilimumab

1 and nivolumab, right?
2 A I see where it says "some monoclonal
3 antibodies targeting these molecules." I
4 don't see the words "ipilimumab" and
5 "nivolumab" right now, but I'm assuming that
6 that's what's referenced in References 58
7 through 60.
8 Q Okay. And you can take a look at the
9 references. So you can go towards the end of
10 the article. You'll see the references for
11 58 through 60, right?
12 A Yes. 58 is ipilimumab. 59 is the
13 combination of nivolumab plus ipilimumab.
14 And 60 is pembrolizumab.
15 Q Okay. And so the POSA would have seen
16 in Pernot a specific reference to the
17 checkpoint inhibitors ipilimumab, nivolumab
18 and pembrolizumab; right?
19 A That's correct.
20 Q And nivolumab is the checkpoint
21 inhibitor that was posted on
22 clinicaltrials.gov for a clinical trial in

1 MSI-High patients before JHU even applied for
2 the patent at issue in this case, right?
3 A My memory is that that trial was an
4 exploratory trial of a set of rare diseases,
5 and one of those rare diseases was MSI-High
6 cancer.
7 Q Okay. So let me try my question again.
8 Would you agree that nivolumab is the
9 checkpoint inhibitor that was posted on
10 clinicaltrials.gov for a clinical trial in
11 MSI-High patients before JHU even applied for
12 the patent at issue in this case?
13 A Well, I don't have that in front of me,
14 so I don't recall the dates.
15 Q Okay. Do you recall the dates when JHU
16 applied for a patent in this case?
17 A The first priority date, is that what
18 you're asking for?
19 Q Yeah.
20 A Was the first priority date? I don't
21 recall the exact date. My memory is it's in
22 2013.

1 Q You have your declaration in front of
2 you, right?
3 A I have it, yes.
4 Q Can you turn to Paragraph 8 of your
5 declaration. And then can you read that to
6 yourself and let me know when you're
7 finished.
8 A Yes. Finished.
9 Q Okay. And does that refresh your
10 recollection as to when JHU first applied for
11 the patent at issue in this case?
12 A Yes.
13 Q And that date was November 13, 2014; is
14 that right?
15 A That's correct.
16 Q Okay. Let me turn your attention to an
17 exhibit. It's Exhibit 1053.
18 (Whereupon, Study NCT02060188,
19 dated 2-10-14 was marked as
20 Exhibit 1053 for identification
21 as of this date.)
22 Q We can put that in the chat, and you can

1 take a look at it.
2 TECH WELCH: 1053 uploading now. It
3 may be just a moment.
4 A Yes.
5 Q Okay. Now, you see that Exhibit 1053 is
6 a study record for nivolumab?
7 A Yes.
8 Q And do you see that Exhibit 1053 is the
9 February 10, 2014 version of that study
10 record?
11 A Yes.
12 Q And so would you agree with me that
13 nivolumab is the checkpoint inhibitor that
14 was posted on clinicaltrials.gov for a
15 clinical trial in MSI-High patients before
16 JHU even applied for the patent at issue in
17 this case?
18 MR. MILLER: Objection. Scope.
19 A Yes.
20 Q And before the critical date, July 10,
21 2015, pembrolizumab was publicly known to be
22 an immunotherapeutic, right?

1 A Yes.
2 Q And before the critical date,
3 pembrolizumab was publicly known to be a
4 checkpoint inhibitor, right?
5 A Yes.
6 Q Would you agree with me that before the
7 time of the critical date, July 10, 2015,
8 there were publications that discussed the
9 treatment of colorectal cancer patients in
10 clinical trials?
11 A I'm sorry. Could you repeat the
12 question?
13 Q Sure.
14 Would you agree with me that before the
15 critical date there were publications that
16 discussed the treatment of colorectal cancer
17 patients in clinical trials?
18 A Yes.
19 Q And would you agree that the Benson
20 publication that you read in this case was
21 about colorectal cancer patients?
22 A The Benson publication. Can you remind

1 what the Benson publication is?
2 Q Sitting here right now, you don't
3 remember Benson?
4 A It sounds familiar, but I don't remember
5 which particular paper Benson was.
6 Q Okay. Let's take a look at
7 Exhibit 1009.
8 TECH WELCH: 1009 is uploading now.
9 (Whereupon, "Colon Cancer,
10 Version 3.2014, Clinical
11 Practice Guidelines in
12 Oncology," published July 2014
13 was marked as Exhibit 1009 for
14 identification as of this date.)
15 Q Just let me know when you have the
16 exhibit, sir.
17 A Yes, I have it.
18 Q And this is the publication that you
19 read as part of your work in this case?
20 A Yes.
21 Q Okay. And would you agree that the
22 Benson publication that you read as part of

1 your work in this case was about colorectal
2 cancer patients?
3 A Yes.
4 Q And the publication was specifically
5 about clinical practice guidelines, right?
6 A That is correct.
7 Q Now, when you read the Benson
8 publication, you read it objectively, right?
9 A Yes.
10 Q You didn't add any bias to your read of
11 Benson, right?
12 A No.
13 Q And you understand that Benson gave a
14 summary of the then in place national
15 comprehensive cancer network clinical
16 practice guidelines in oncology for managing
17 metastatic colorectal cancer, right?
18 A Yes.
19 Q And Benson explains that the guidelines
20 are believed to represent the optimal
21 treatment strategy, right?
22 A Yes.

1 Q And you agree that the then NCC
2 guidelines recommended including clinical
3 studies as a therapy for metastatic cancer
4 patients who had a third progression or more
5 of their cancer, right?
6 A I don't recall that.
7 Do you want me to the find it?
8 Q Sure.
9 A Do you want to point me to the language?
10 Q Well, I'm asking the question, but you
11 can turn your attention to Page 7 of the
12 exhibit to see if it's helpful to responding
13 to my question.
14 A Yes.
15 Q "Yes" is the answer to my question?
16 A Yes. Regorafenib, if not given
17 previously or clinical trial or best
18 supportive care.
19 Q Now, before the critical date, July 10,
20 2015, you would agree with me that
21 pembrolizumab was administered to patients
22 intravenously, right?

1 A Yes.
2 Q And before the critical date, you agree
3 that there were publications that discuss
4 intravenous administration of pembrolizumab,
5 right?
6 A Yes.
7 Q And one of those publications that you
8 read as part of this case was a 2013 article
9 by Hamid, right?
10 A Yes.
11 Q And when you read the Hamid article, you
12 read it objectively, right?
13 A Yes.
14 Q You didn't try to add any bias into your
15 reading of Hamid, right?
16 A No.
17 Q You understand that the Hamid Group was
18 providing to the public results of a clinical
19 study of pembrolizumab in patients with
20 measurable metastatic or locally advanced
21 unresectable melanoma, right?
22 A That's my memory.

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

1 authors write about what their study
2 confirms?
3 A Yes.
4 Q And you would agree with the Hamid
5 Group's assessment that their clinical study
6 confirms the importance of releasing
7 inhibitory immune regulation by PD-1 for
8 respective antitumor immunity, right?
9 A That's correct.
10 Q That would have been knowledge of the
11 person of ordinary skill in the art at the
12 time the study record was posted, right?
13 A That is correct.
14 Q You understand that the Hamid Group
15 explained to the public that they
16 administered pembrolizumab to patients
17 intravenously, right?
18 A That is correct.
19 Q You understand that the Hamid Group
20 explained to the public that they
21 administered pembrolizumab at a dose of
22 10-milligrams per kilogram every two or

1 three weeks, right?
2 A I know it was 10-milligrams per
3 kilograms for two or three weeks. Yes, they
4 compared, two weeks versus three weeks.
5 Q Okay. And the POSA at the time of the
6 posting of the study record would have seen
7 in the Hamid article the specific mention of
8 administering pembrolizumab intravenously,
9 right?
10 Let me try that again. Tongue twister.
11 You would agree that the POSA, at the
12 time of the posting of the study record,
13 would have seen in the Hamid article the
14 specific mention of administering
15 pembrolizumab intravenously, right?
16 A That's correct.
17 Q Now, before the critical date, July 10,
18 2015, there were publications that concluded
19 that high levels of mutational heterogeneity
20 in a tumor could be the key for success of
21 immune checkpoint targeting, right?
22 A I'm sorry. Can you just repeat that one

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

1 checkpoints efficacy," published
2 January 2014 was marked as
3 Exhibit 1032 for identification
4 as of this date.)
5 A I have it.
6 Q So you recall reading the Champiat 2014
7 publication, right?
8 A Yes.
9 Q If I can turn your attention to the
10 first page of this exhibit. And so you see
11 where they formulate a hypothesis?
12 A At the very top of the page, on the
13 right-hand column, "These observations may
14 suggest that the mutational heterogeneity of
15 the tumor could be the key of the success of
16 immune checkpoint targeted therapy."
17 Q Right. And so this is a publication
18 from 2014, right?
19 A That is correct.
20 Q So this is before the critical date in
21 this case, right?
22 A That is correct.

1 Q Let me ask my question, just to make
2 sure it's clear.
3 Before the critical date, there were
4 publications that concluded that high levels
5 of mutational heterogeneity in a tumor could
6 be the key for success of immune checkpoint
7 targeting, right?
8 MR. MILLER: Objection, form.
9 A This is not a conclusion, this is a
10 hypothesis.
11 Q Right. So you -- okay. Well, you agree
12 that before the critical date there were
13 publications that were proposing that high
14 levels of mutational heterogeneity in a tumor
15 could be the key for success of immune
16 checkpoint targeting, right?
17 A That was a hypothesis. And there are
18 many hypotheses that turned out to be wrong,
19 as I alluded to before the concept of
20 depleting regulatory T cells for treating
21 MSI-High tumors has not been proven.
22 Q Okay. Well, you would agree that the

1 POSA would have knowledge of the Champiat
2 Group's observation of a significant
3 association between mutational load of tumors
4 and their susceptiblity to PD-1, PDL1
5 targeting agents, right?
6 MR. MILLER: Objection, form.
7 A You just mixed up two very different
8 concepts. One is mutational load and the
9 other one is mutational heterogeneity.
10 Q I don't think I did anything of the
11 sort. So let me ask my question.
12 Would you agree that the person of
13 ordinary skill would have knowledge of the
14 Champiat Group's observation of a significant
15 association between the mutational load of
16 tumors and their susceptibility to PD-1, PDL1
17 targeting agents?
18 A The sentence here refers to observations
19 by others. And then the Champiat Group is
20 proposing hypothesis that suggests it's
21 mutational heterogeneity and not mutational
22 load.

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

1 into the third column.
2 A As a hypothesis generated case we
3 observed a significant association between
4 the mutational load of tumors and their --
5 okay. So they're observing basically based
6 on data by others. And that's Figure 1. And
7 I think Figure 1 is kind of key to explaining
8 their hypothesis because it's not linear
9 with -- the responses to checkpoint blockade
10 are not linear with mutational load. And
11 that's why kidney cell cancer stands out.
12 And it's why DLBCL and ovarian and
13 glioblastoma don't respond to checkpoint
14 blockade. And they all have higher
15 mutational load than RCC, and all much
16 higher, RCC has much higher mutational load
17 than, say, polyomavirus positive Merkel cell
18 carcinoma. And yet polyomavirus positive
19 Merkel cell carcinoma responds to checkpoint
20 blockade.
21 So there's kind of this nonlinearity,
22 and then they come up with hypothesis that I

1 think it's an interesting hypothesis, but it
2 is just a hypothesis, that is that it's
3 mutational heterogeneity.
4 Q And what question were you answering? I
5 just want to make sure the record is clear.
6 A I was trying to explain what their
7 observation referred to.
8 Q Okay. Okay. So my question is
9 different.
10 Would you agree that the person of
11 ordinary skill would have knowledge of the
12 Champiat Group's observation of a significant
13 association between mutational load of tumors
14 and their susceptibility of PD-1, PDL1
15 targeting agent?
16 A Yeah. That's what's written in their
17 paper, yes. And that is referring to
18 Figure 1.
19 Q And the POSA would also understand --
20 A Figure 1 highlights the discordance.
21 And that's the reason I think why they came
22 up with this hypothesis of mutational

1 heterogeneity, and then they proposed testing
2 that hypothesis.
3 Q Now, Doctor, would you also agree that
4 the POSA would understand, at least from the
5 Champiat paper, that DNA mismatch repair
6 deficient tumors including MSI-High
7 colorectal cancer displayed severe genomic
8 instability?
9 A Yes.
10 Q Would you agree that Champiat recommends
11 evaluating the clinical activity of PD-1,
12 PDL2 agents in MSI-High colorectal cancer?
13 A Well, they have a sort of a step wise --
14 their sentences -- their proposal is kind of
15 step wise. They propose basically testing
16 their hypothesis about mutational
17 heterogeneity, not mutational load, and that
18 if that is correct, then it would be
19 interesting to test checkpoint blockade in
20 MSI-High patients.
21 Q Let me try my question again. I
22 actually don't think it was framed in the

1 right way. So I want to help you.
2 Would you agree that Champiat recommends
3 evaluating the clinical activity of PD-1,
4 PDL-1 agents in MSI-High colorectal cancer?
5 A But there's a caveat in the paper, the
6 actual sentence is moreover if high levels --
7 if high levels of mutational heterogeneity
8 increase the tumor immunogenicity it will be
9 interesting. So they are implicitly
10 proposing testing that hypothesis and then if
11 that hypothesis is true then it would be
12 interesting to evaluate the clinical activity
13 of PD-1, PDL-1 agents. In fact, shortly
14 after the critical date there was a set of
15 experiments that were done and an analysis
16 from a group in the UK Swanton et al., where
17 they showed, in fact, mutational
18 heterogeneity was not the key. That, in
19 fact, it was a requirement for successful
20 checkpoint blockade therapy with clonal
21 mutations and not heterogeneous mutations.
22 So, in fact, the entire hypothesis of

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

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

1 Dr. Rosenberg's group where they found that a
2 clonal T-cell transfusion could drive an
3 effective antitumor response in a patient.
4 Q Okay. So I understand you have
5 positions, Doctor, but I just want an answer
6 to my question.
7 Just to be clear. I asked you, do you
8 believe it is appropriate to rely upon a
9 reference from after the critical date in
10 making an assessment as to whether or not any
11 of the claims of the '393 Patent are obvious?
12 MR. MILLER: Objection. Form.
13 Q What's the answer to that question?
14 MR. MILLER: Objection. Asked and
15 answered. Go ahead.
16 A No. And that's why I then came back
17 with a set of articles that a person of
18 ordinary skill in the art would be aware of
19 that were prior art prior to the July 10,
20 2015 date.
21 Q Now, before the critical date, would you
22 agree that there were publications stating

1 that PD-1, PDL-1 were differently expressed
2 in molecular subtypes of colon cancer
3 pointing to MSI-High and MSS cases?
4 MR. MILLER: Objection. Form.
5 A Yes.
6 Q Okay. From one of those publications
7 was a 2014 article by Dr. Gatalica, right?
8 A I would have to go back and look at
9 that.
10 Q Do you recall reading an article by
11 Dr. Gatalica in this case?
12 A I -- it sounds familiar, but I would
13 want to go back and make sure that I'm
14 thinking of the right paper.
15 Q Okay. Would you agree that before the
16 critical date there were publications stating
17 the patients showing naturally immunogenetics
18 mutation associated with tumor infiltrating
19 lymphocytes are potential candidates for
20 treatment with immune modulators such as
21 PDCD-1 targeted antibody?
22 A That sounds correct, my recollection is

1 that that would have been in the literature,
2 yes.
3 Q Okay. Would you agree that before the
4 posting of the study record there were
5 publications noting that MSI is a common
6 molecular classifier of colon cancer, right?
7 A That's correct.
8 Q Now, would you agree that years before
9 the posting of the MSI-High study records,
10 there were publications describing that
11 colorectal cancers with Microsatellite
12 Instability are characterized by tumor
13 infiltrating lymphocytes and have a good
14 prognosis?
15 A Yes.
16 Q Now, before the posting of the study
17 records you would agree that there were
18 publications explaining the tumor
19 infiltrating T-cells may be an indicator of
20 post immune response to tumor and an
21 attractive target for immunotherapy, right?
22 A Yes.

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

1 marked as Exhibit 1039 for
2 identification as of this date.)
3 Q And do you recall reading Exhibit 1039
4 as part of your work on this case?
5 A Yes.
6 Q And this is the publication by Llosa; is
7 that right?
8 A Yes, yes.
9 Q Okay. And would you agree that before
10 the critical date, the Llosa Group were
11 telling the public that a strong inflammatory
12 response in MSI colorectal patients triggered
13 the expression of PDL-1, which could be
14 targeted to enhance clinical benefit and be
15 predictive of response to immune checkpoint
16 inhibitors?
17 A Yes. It actually says on PDL-1 and
18 IDL-1.
19 Q It's both, right?
20 A Yes.
21 Q Your read of Llosa, as part of this
22 case, you gave it an objective read, right?

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

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

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

1 publications stating that MSI-High colorectal
2 cancer patients may have greater responses to
3 checkpoint blockade therapy?
4 A Well, that's a very specific wording
5 that you gave, and I don't have an opinion as
6 to whether that particular sentence was out
7 there in the literature, so I'd like to see
8 what you're referring to.
9 Q Okay. And I wasn't referring to a
10 particular sentence and I am trying to be
11 precise in my question. So let me try it
12 again.
13 Would you agree that prior to the
14 critical date there were publications
15 explaining that MSI-High colorectal cancer
16 patients may have greater responses to
17 checkpoint blockade therapy?
18 A You said may, so you're talking about
19 with the hypothesis out there. Yes, the
20 hypothesis is out there.
21 Q Now, before the July 10, 2015, critical
22 date, you are aware that Dr. Gatalica that we

1 mentioned earlier, publicly reported that
2 there were more than five PD-1, PDL-1
3 clinical trials were ongoing, do you recall
4 that?
5 A I don't recall that part of the
6 publication. Should I pull it up, again?
7 Q We can pull up Exhibit 1084.
8 (Whereupon, "Caris Life Sciences
9 Research Provides Key Clinical
10 Insights on Immunotherapeutic
11 Targets in a Broad Range of
12 Cancers," dated 6-10-14 was
13 marked as Exhibit 1084 for
14 identification as of this date.)
15 A Okay. I have it.
16 Q Do you recognize Exhibit 1084 as a
17 document that you referred to in your October
18 4, 2024, declaration?
19 A I may have. I would have to look at my
20 declaration to see if this is a document.
21 Q And sitting here today, right now, you
22 just don't have a recollection of whether or

1 not you referred to Exhibit 1084 in your
2 declaration?
3 A I don't want to -- I don't want to go
4 beyond my recollection, which is why I'd like
5 to see if this is the specific document.
6 Q And, sir, to be clear I'm not asking you
7 to go beyond your recollection, I'm asking
8 that very question. Sitting here right now,
9 in this moment, do you have a recollection,
10 one way or the other, if you actually refer
11 to Exhibit 1084 in your October 4, 2024,
12 declaration?
13 A I have a recollection, but it's not a
14 specific recollection, and that's why I would
15 like to make sure that this is the correct
16 document.
17 Q Fair enough. Do you recall reviewing
18 Exhibit 1084?
19 A I would like to -- it looks familiar,
20 but I would like to make sure that this is
21 the same document that I reviewed.
22 Q Do you have your October 4, 2024,

1 declaration in front of you?
2 A Yes.
3 Q Let me turn your attention to Page 80 of
4 your declaration.
5 Do you see that you have a citation to
6 Exhibit 1084?
7 A Oh, yes, yeah.
8 Q Does this refresh your recollection that
9 you looked at Exhibit 1084?
10 A Yes. But I want to look for that
11 particular language that will refresh my
12 memory.
13 Q Which particular language are you
14 looking for?
15 A The language in my declaration.
16 Q Let me know if you see it.
17 A Yes. I found it. That's -- that is the
18 article that I reviewed, yes.
19 Q And when you reviewed it, you reviewed
20 it carefully?
21 A Yes.
22 Q And would you agree that before the

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

1 POSA would have had as of the time of the
2 critical date, right?
3 A Correct.
4 Q Now, would you agree that by the time of
5 the critical date, July 10, 2015, there was
6 another clinical trial about administering an
7 anti-PD-1 inhibitor to MSI-High colorectal
8 cancer patients?
9 A Which trial are you referring to?
10 Q How about the trial involving nivolumab?
11 A Yes.
12 Q So you would agree that by the time of
13 the clinical date there was another clinical
14 trial about administering an anti-PD-1
15 inhibitor to MSI-High colorectal cancer
16 patients, right?
17 A Correct.
18 Q And you would agree that there was a
19 clinicaltrial.gov posting by the time of the
20 critical date about that other clinical trial
21 involving administration of an anti-PD-1
22 inhibitor to MSI-High colorectal cancer

1 patients, right?
2 A Correct.
3 Q And that nivolumab trial about
4 administering an anti-PD-1 inhibitor to
5 MSI-High cancer patients was sponsored by
6 BMS, correct?
7 A That's correct.
8 Q BMS is that Bristol Myers Squibb, am I
9 right?
10 A That's correct.
11 Q And at the time of the study records
12 posting for this nivolumab trial involving a
13 study of an anti-PD-1 inhibitor to MSI-High
14 colorectal cancer patients, you were working
15 at BMS, right?
16 A That's correct.
17 Q And you would agree that the purpose of
18 this trial conducted by BMS was to examine if
19 nivolumab alone or in combination with
20 ipilimumab would demonstrate a meaningful
21 objective response rate in patients with
22 recurrent and metastatic colon cancer who

1 also have a specific biomarker in their
2 tumors, right?
3 MR. MILLER: Objection. Form.
4 A Who also have a specific biomarker, is
5 that what you said?
6 Q Who also have a specific biomarker in
7 their tumors?
8 A A biomarker beyond MSI-High.
9 Q Let me try my question again.
10 A Can we go to that study record.
11 Q Sure. We looked at it before, I think
12 it's Exhibit 1053.
13 Do you have it, sir?
14 A Yes.
15 Q Okay. And you would agree that prior to
16 JHU even applying for the patent at issue in
17 this case, BMS had publicly posted this study
18 record explaining that the purpose of the
19 study is to examine whether nivolumab alone
20 or in combination with ipilimumab would
21 demonstrate a meaningful objective response
22 rate in patients with recurrent and

1 metastatic colon cancer who also have a
2 specific biomarker in their tumors, right?
3 A That's correct.
4 Q Was that specific biomarker that BMS was
5 referring to MSI positive?
6 A MSI positivity, yes.
7 Q And you would agree that as of
8 February 10, 2014, BMS considered their study
9 number NC202060188 worth performing, right?
10 A Correct.
11 Q And you would agree that as of the
12 critical date in this case, BMS considered
13 their study number NCT2060188 worth
14 performing, right?
15 A Yes. And we actually performed many
16 clinical trials that failed. So considered
17 worth performing was not an indication of
18 successful outcome.
19 I wish it was.
20 Q Now, the study that we've been referring
21 to No. NCT02060188, this is the study
22 involving nivolumab and MSI-High colorectal

1 cancer patients, right.?
2 A MSI-High colorectal cancer patients are
3 included in the study, yes.
4 Q Do you recall using the phrasing in your
5 declaration --
6 Let me try this again.
7 Do you recall using the phrasing in your
8 October 4, 2024, declaration, "worth
9 performing" as it relates to a clinical
10 study.
11 A Can you point me to the language?
12 Q Well, I'm just asking, sitting here
13 today, without looking at your declaration,
14 do you have any recollection whatsoever if
15 you ever used the phrase "worth performing"
16 in the context of a clinical study?
17 A I've used that phrase many times in my
18 life, I don't remember if that is a phrase
19 that I used in this particular declaration.
20 Q Okay. So looking at your October
21 4, 2024, declaration you can turn your
22 attention to Paragraph 186.

1 Let me know when you have it.
2 A I have it.
3 Q And you see in the first sentence of
4 your declaration you testified "Prior to the
5 actual release of JHU's trial results there
6 was substantial skepticism from experts that
7 such a study was worth performing."
8 Do you see that?
9 A That's true.
10 Q And the study that you're talking about
11 is a study that was disclosed in the posted
12 MSI study record, right?
13 A That's true.
14 Q When you say the actual release of the
15 JHU's study results, what data are you
16 talking about there?
17 A The publication in the New England
18 Journal paper.
19 Q You're talking about May 30th, 2015?
20 A Is that when it was published, I don't
21 remember.
22 Q Okay. Well, you would agree with me

1 that as of the February 2014, publication
2 date of the study record for the BMS
3 NCT2060188 study involving nivolumab, BMS
4 considered that study worth performing,
5 right?
6 A I agree.
7 Q Now, you're not taking the position in
8 this case that BMS passed up an opportunity
9 to study pembrolizumab in MSI-High colorectal
10 cancer patients, right?
11 A BMS was not in a position to or would
12 not would have wanted to study pembrolizumab.
13 BMS would have wanted to study nivolumab.
14 Q I just want to be clear. So you are not
15 taking the position, in this case, that BMS
16 passed up an opportunity to study
17 pembrolizumab in MSI-High colorectal cancer
18 patients, right?
19 A Correct.
20 Q And you do agree that prior to the
21 critical date in this case, BMS did take the
22 opportunity to sponsor a study involving an

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

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

1 A I believe that's correct.
2 Q So would you agree with me that -- let
3 me ask it this way.
4 Would you agree that by the critical
5 date in this case JHU had initiated it's own
6 work to conduct a clinical trial in MSI-High
7 patients involving an anti-PD-1 therapy?
8 A I believe the answer to your question is
9 yes, but I want to make sure I understand
10 your question correctly, so could you repeat
11 it.
12 Q Do you appreciate -- yeah, let me make
13 sure my question --
14 Do you appreciate that by the critical
15 date, in this case, BMS had initiated its own
16 work to conduct a clinical trial in MSI-High
17 patients involving an anti-PD-1 therapy?
18 A Yes.
19 Q And would you agree that BMS took the
20 opportunity to perform a study of an
21 anti-PD-1 therapy in MSI-High colorectal
22 cancer patients prior to the actual release

1 of the trial results from the study disclosed
2 in the MSI-High study record that we've been
3 discussing today?
4 A Yes. Bristol Myers changed their mind
5 about the value of conducting such a trial.
6 That doesn't mean that they were certain of
7 the outcome, but they changed their mind
8 about the value and I think once the data
9 came out from Johns Hopkins they regretted
10 having made that initial decision not to
11 partner with Johns Hopkins.
12 Q Now, this trial involving nivolumab
13 NCT2060188, you refer to that trial in your
14 October 4, 2024, declaration as a
15 contemporary trial to the trial identified in
16 the study record, right?
17 A They overlapped.
18 Q I didn't ask if they overlapped. My
19 questions different.
20 The BMS study involving nivolumab with
21 the number NCT2060188, is a trial that you
22 refer to in your sworn declaration as a

1 contemporary trial to the trial identified in
2 the study record we've been discussing today,
3 right?
4 A Yes. And I said that they overlap, I
5 think that's a similar meaning.
6 MR. MILLER: Preston, we've been going
7 well over an hour, is this a good
8 break time.
9 MR. RATLIFF: Would you like to take a
10 break, Dr. Lonberg?
11 THE WITNESS: Yes. Please.
12 MR. RATLIFF: Okay. Let's take a
13 break.
14 (Whereupon, a recess was taken
15 from 5:56 PM until 6:09 PM.)
16 BY MR. RATLIFF:
17 Q Doctor, can you look at the study record
18 for the BMS nivolumab study, this is
19 Exhibit 1053.
20 A Okay, yes.
21 Q And actually before we do that, at any
22 point in time today during the breaks did you

1 discuss your deposition testimony?
2 A I made an offhand hallway comment about
3 the style of the deposition.
4 Q Okay. And at any point in time during
5 any of the breaks today, did you discuss this
6 case?
7 A No.
8 Q So let's take a look at the study
9 record, this is Exhibit 1053.
10 And you would you agree that the POSA
11 would have seen posted the official title of
12 this study, right?
13 A Yes.
14 Q And the official title of the study of
15 nivolumab, and nivolumab plus ipilimumab in
16 recurrent metastatic colon cancer; is that
17 right?
18 A The official title is a Phase II
19 clinical trial of nivolumab and nivolumab
20 plus ipilimumab in recurrent and metastatic
21 microsatellite-High, MSI-H colon cancer.
22 Q Thank you. And when you reviewed the

1 '393 Patent at Page 2, that refers to this
2 version of the study record, right?
3 A Are you talking about references.
4 Q I'm talking about if you go to the '393
5 Patent.
6 A Yes.
7 Q And you looked at Page 2, right?
8 A And by Page 2 you --
9 Q The second page of the patent.
10 A Right. It's just the patent starts out
11 with references cited and then it goes into
12 figures, are you talking about that as the
13 page number or are you talking about the
14 beginning of Column 1 and Column 2.
15 Q Right. So I'm talking about the section
16 that says references cited on Page 2, so not
17 the column to the patent, but where it
18 actually says Page two.
19 A Yes.
20 Q Okay. And you see there's a section
21 entitled other publications?
22 A Yes.

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

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

1 of ordinary skill would have been aware of
2 both the BMS clinical trial involving an
3 anti-PD-1 inhibitor and MSI colorectal cancer
4 patients, as well as the trial that's
5 disclosed in the study record, Exhibit 1005?
6 A Yes.
7 Q So you would agree with me that prior to
8 the critical date in this case, the POSA
9 would have been aware of at least two
10 clinical trials testing an anti-PD-1
11 inhibitor in MSI-High colorectal cancers,
12 right?
13 A Correct.
14 Q And the publication of the BMS study
15 record came about nine months before JHU even
16 filed it's first professional application
17 relating to the '393 Patent, right?
18 A Yes.
19 Q And that publication of the BMS study
20 record came more than 17 months before the
21 critical date in this case, right?
22 A Yes.

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

1 posted on clinicaltrial.gov you also didn't
2 write to anyone at the FDA expressing
3 skepticism that the study was worth
4 performing, right?
5 A No.
6 Q And when the study record was published
7 on clinicaltrials.gov you also didn't write
8 to anyone at Merck expressing skepticism that
9 the study was worth performing, right?
10 A No. Of course not.
11 Q And when the study record was published
12 on clinicaltrials.gov, you didn't write to
13 anyone at all expressing skepticism that the
14 study was worth performing, right?
15 A No.
16 Q Are aware of anyone ever writing to JHU
17 expressing skepticism that the study
18 disclosed in the study record was not worth
19 performing?
20 A No.
21 Q Are you aware of anyone ever writing to
22 the FDA that the study disclosed in the study

1 record was not worth performing?
2 A No.
3 Q Are you aware of anyone ever writing to
4 the NIH that the study disclosed in the study
5 record was not worth performing?
6 A No.
7 Q Are you aware of anyone ever writing to
8 clinicaltrials.gov, stating that the study
9 record was not -- let me try that again.
10 Are you aware of anyone ever writing to
11 clinicaltrials.gov, that the study records
12 disclosed -- I'm sorry, let me try this
13 again.
14 Are you aware of anyone ever writing to
15 clinicaltrials.gov, that the trial disclosed
16 in the study record was not worth performing?
17 A No.
18 Q Are you aware of anyone ever calling the
19 FDA, clinicaltrials.gov, the NIH, or anyone
20 to state that the trial that's disclosed in
21 the study record was not worth performing?
22 A No.

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

1 Q And Drew Pardoll -- excuse me?
2 A That's my memory.
3 Q That's your memory.
4 And Drew Pardoll is one of the named
5 inventors on the '393 Patent, right?
6 A Yes.
7 Q And is it fair to say that Drew Pardoll
8 has an interest in the outcome of this case?
9 A Yes.
10 Q Now, you understand that at the time
11 that the study record was posted,
12 Exhibit 1005, that Merck was a collaborator
13 for that study, right?
14 MR. MILLER: Objection. Form.
15 A I don't know that that would be clear
16 from the study record. I know now that they
17 provided a drug for free. They provided
18 pembrolizumab.
19 Q It's your understanding that Merck
20 provided drug for free to John Hopkins to
21 conduct the study that's disclosed in the
22 study record?

1 A That's standard practice. Many drug
2 companies have programs like that, and Merck
3 has -- they still have an active program
4 where they will provide pembrolizumab for
5 free for clinical studies. Obviously, they
6 have restrictions on how you share the data,
7 but they provide the drug. That's quite
8 common.
9 Q Okay. I'm not asking anything about
10 standard practice. I'm asking specifically
11 about Merck.
12 A Yeah, well, this is about Merck. I'm on
13 the board of a company right now where we've
14 gotten study drug from Merck. We've gotten
15 pembrolizumab from Merck.
16 Q Okay. And so here's my question: Is it
17 your understanding that Merck provided
18 pembrolizumab for free to John Hopkins as
19 part of conducting the clinical trial that's
20 described in the study record, Exhibit 1005?
21 A That is my current understanding, but I
22 don't know when I came to that understanding.

1 Q Okay. And the study record, did you
2 review that carefully?
3 A The study record, yes.
4 Q Yes.
5 Did you?
6 A Yes.
7 Q Okay. And do you recall whether or not
8 the study record indicated that Merck was a
9 collaborator for the study?
10 A Well, let me go look at it. What's the
11 number again?
12 Q Well, I was asking -- I was asking you,
13 sitting here today, do you have any
14 recollection one way or not if Merck was
15 indicated as the collaborator in that study
16 record?
17 A Yes. They're indicated as a
18 collaborator.
19 Q Okay. And as a collaborator, you
20 understand that Merck had provided support to
21 conduct the clinical study that's described
22 in the study record, right?

1 MR. MILLER: Objection. Form. Scope.
2 A I don't -- I wouldn't have known what
3 the level of collaboration would be in
4 this -- from the study record. It could have
5 been everything from supplying drug to
6 analyzing biopsies. There's a number of
7 different ways that drug companies
8 collaborate with institutional investigators.
9 Q Right. And for the study that's
10 described in the study record that we've been
11 discussing, sitting here today, you don't
12 have any knowledge of the extent of the
13 support that Merck provided, right?
14 A I have some knowledge in that they
15 provided drug.
16 Q But beyond that, do you have any
17 additional knowledge as to what support Merck
18 provided as part of that study?
19 A Not that I can recall.
20 Q You have a copy of the '393 Patent,
21 right, sir?
22 A Yes.

1 Q And can you turn your attention to the
2 claims of the '393 Patent.
3 A Yes.
4 Q And looking at Claim 1, would you agree
5 that all that Claim 1 requires in terms of
6 success is treating a colorectal cancer
7 patient, right?
8 A With mismatch repair deficient --
9 deficiency, or --
10 Q Okay. Let me try that again.
11 So you would agree that in terms of
12 success, all that Claim 1 of the '393 Patent
13 requires is treating a MSI-High colorectal
14 cancer patient with pembrolizumab, right?
15 A Right. But you wouldn't be able to
16 treat an MSI-High or dMMR deficient patient
17 unless you had first identified that patient
18 by testing and then, in response to the
19 outcome of that test, treating.
20 Q And in your opinion, is there any
21 requirement set forth in Claim 1 of the
22 '393 Patent as to how well the colorectal

1 cancer patient has been treated?
2 MR. MILLER: Objection. Form.
3 A It says "therapeutically effective."
4 Q Well, it says you have to give a
5 therapeutically effective amount of
6 pembrolizumab, right?
7 A Right.
8 Q But do you have any opinion with respect
9 to Claim 1 if there's any level of treatment
10 required to the MSI-High colorectal cancer
11 patient beyond simply treating the patient?
12 MR. MILLER: Objection. Form.
13 A I don't understand what you mean by "any
14 level of treatment."
15 Q Do you have any opinion as to the extent
16 of treatment that's required by Claim 1 of
17 the '393 Patent to a colorectal cancer
18 patient?
19 MR. MILLER: Objection. Form.
20 A You mean the -- the length of time that
21 the patient is treated?
22 Q I mean the outcome that would happen --

1 A Oh.
2 Q -- for the cancer patient?
3 A I see.
4 MR. MILLER: Let me just -- objection.
5 Form.
6 A I completely misunderstood your
7 question. I apologize.
8 Q No worries.
9 A So what you're asking -- now rephrase
10 your question again now that I understand
11 what you meant by the level.
12 Q Right. So looking at Claim 1, do you
13 have any opinion as to the -- if Claim 1 has
14 a required outcome for the treatment that's
15 called for by Claim 1?
16 MR. MILLER: Objection. Form.
17 A All I can say is that it is implied
18 because the patient is treated with a
19 therapeutically effective amount of
20 pembrolizumab.
21 Q An effective to accomplish what?
22 A Patient benefit.

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

1 break, and let me see what I can do.
2 THE WITNESS: Okay.
3 (Whereupon, a recess was taken
4 from 6:32 PM until 6:45 PM.)
5 Q Doctor, during the break did you discuss
6 any of your testimony today?
7 A No.
8 Q And, Doctor, during the break did you
9 discuss this case at all?
10 A No.
11 Q Doctor, would you agree that the BMS
12 MSI-High nivolumab trial that you refer to as
13 a contemporary trial of the trial disclosed
14 in the MSI-High study record was not a failed
15 trial?
16 A I don't remember the outcome of the
17 trial. I don't remember the data.
18 Q Sitting here today, you don't --
19 A I don't recall the data, no.
20 Q And so just to be clear, do you recall
21 whether or not the trial was considered a
22 success, the BMS MSI-High nivolumab trial?

1 A I don't remember what the outcome was.
2 Q Okay. And do you know one way or not
3 whether the FDA granted nivolumab accelerated
4 approval for MSI-High colorectal cancer based
5 on the NCT2060188 BMS study?
6 A No. I don't recall.
7 Q Okay. You don't have a recollection.
8 So since you don't have a recollection
9 maybe we can take a look at a new exhibit,
10 and it's Exhibit No. 1120.
11 MR. RATLIFF: This is a new exhibit
12 that we're introducing.
13 (Whereupon, "FDA grants
14 nivolumab accelerated approval
15 for MSI-H or dMMR colorectal
16 cancer" was marked as Exhibit
17 1120 for identification as of
18 this date.)
19 Q And similar to the others, let me know
20 when you have it, Doctor.
21 TECH WELCH: 1120 is uploading.
22 MR. MILLER: Keli, can you tell if

1 it's uploaded?
2 TECH WELCH: I will double-check.
3 MR. MILLER: I'm not seeing it yet.
4 Q And you have the new exhibit, 1120,
5 Doctor?
6 A Yes, I do.
7 Q And you testified earlier that just
8 sitting at that time when I asked you the
9 question, you had no recollection of whether
10 or not the BMS MSI-High colorectal cancer
11 trial that we have been discussing,
12 NCT2060188, was a success or failure; is that
13 right?
14 A That's correct.
15 Q Okay. And I've placed in front of you
16 new Exhibit 1120, which is a press release
17 taken from the FDA's website that I can
18 represent to you entitled "FDA grants
19 nivolumab accelerated approval for MSI-High
20 or dMMR colorectal cancer."
21 A Yes. I remember this very well.
22 Q Okay. And you were working at BMS at

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

1 MR. MILLER: You're passing the
2 witness?
3 MR. RATLIFF: I am.
4 MR. MILLER: Thank you.
5 Doctor, I'm going to try to do this
6 without moving us all around.
7 EXAMINATION BY
8 MR. MILLER:
9 Q The rules are the same. Pause after my
10 question to allow counsel to interpose his
11 objection. While this isn't videotaped, may
12 as well keep looking at your screen as you've
13 been doing all day today.
14 Is that all right?
15 A Yes.
16 Q All right. Counsel asked you this, but
17 during the break did we review any of the
18 questions that I was going to pose to you on
19 redirect?
20 A No.
21 Q Did we talk at all about the questions
22 that I might pose?

1 A No.
2 Q All right. You were asked at the
3 beginning of the day a number of questions
4 regarding whether you're an oncologist,
5 right?
6 A Yes.
7 Q And you are not?
8 A No.
9 Q And you're not a medical doctor?
10 A No.
11 Q Could you then explain what it is in
12 your background and experience that qualifies
13 you as a person of ordinary skill in the art
14 in the technology of the '393 Patent as of
15 its critical date?
16 A I have been --
17 MR. RATLIFF: Objection. Beyond the
18 scope.
19 A I have been conducting research in
20 cancer immunotherapy for almost
21 three decades. I -- the very first
22 checkpoint blockade therapy that is now

1 approved to go into the clinic was
2 ipilimumab. That came out of my lab.
3 The second checkpoint blockade target
4 was PD-1. The very first PD-1-targeted drug
5 to go into the clinic that is now approved is
6 nivolumab. That also came out of my lab.
7 The third target -- checkpoint target
8 that has lead to a -- an approved therapy is
9 LAG-3, and that approved antibody is
10 relatlimab, which is a dosing combination
11 with nivolumab, and that came out of my lab.
12 There are now two combination therapies,
13 combination checkpoint blockade therapies
14 that are approved, ipilimumab plus nivolumab
15 and relatlimab plus nivolumab. And both of
16 those combinations came out of my lab.
17 I spent a decade at Bristol Myers
18 Squibb. I was biology head of oncology drug
19 discovery. And for a period of time all
20 early stage cancer clinical trials reported
21 to me, and that included a number of
22 physicians. And I don't think a Fortune 500

1 company would have trusted me to run clinical
2 trials and have physicians reporting to me if
3 they didn't consider me to be at least a
4 person of ordinary skill in the art.
5 Q In 2015, to your knowledge, was
6 pembrolizumab approved for doctors to
7 prescribe to their MSI-High CRC patients?
8 A No.
9 Q Does that fact influence your
10 understanding of what the technical training
11 and/or experience of a person of skill in the
12 art would have had as of July 2015 in the
13 context of the '393 Patent?
14 A Yes.
15 MR. RATLIFF: Objection. Beyond the
16 scope.
17 Q How so?
18 A I think that --
19 MR. RATLIFF: Objection. Beyond the
20 scope.
21 Q You can answer.
22 A I think that, given that this was still

1 an experimental therapy and a non-tested
2 hypothesis, that the important criteria for
3 determining one who is as -- has ordinary
4 skill in the art is going to lean heavily
5 toward experience with an understanding of
6 the basic science, immunology, oncology and
7 an understanding of immunotherapy and an
8 understanding of clinical trial design.
9 Q Thank you.
10 You were also asked by counsel for Merck
11 a number of questions about the study record
12 from 2013, the Hopkins study record, which is
13 Exhibit 1005.
14 Do you recall generally receiving those
15 sorts of questions?
16 A Yes.
17 MR. RATLIFF: Objection. Form.
18 Q I'll start with the time frame of June
19 2013.
20 As of June 2013, would a person of
21 ordinary skill in the art in the field of the
22 '393 Patent have recognized MSI-High as a

1 biomarker or -- yeah, biomarker in colorectal
2 cancer patients for responsiveness to
3 pembrolizumab?
4 A No.
5 Q Before Dr. Le presented her results at
6 the ASCO conference in May of 2015, would a
7 person of skill in the art in the field of
8 the '393 Patent have recognized MSI-High as a
9 biomarker for responsiveness to pembrolizumab
10 in MSI-High colorectal cancer patients?
11 A No.
12 MR. RATLIFF: Objection. Beyond the
13 scope.
14 Q Before the contemporaneous -- before the
15 publication of the New England Journal
16 article, also in May of 2015, and in fact on
17 the same day as the ASCO presentation by
18 Dr. Le; would a person of ordinary skill in
19 the art in the field of the '393 Patent have
20 recognized MSI-High as a biomarker for
21 responsiveness to pembrolizumab in MSI-High
22 colorectal cancer patients?

1 MR. RATLIFF: Objection. Beyond the
2 scope.
3 A No.
4 Q You were asked by counsel for Merck a
5 number of questions about the claims of the
6 '393 Patent, and I have some very short
7 questions about that.
8 If you could take that out and turn your
9 attention to Claims 1 and 14.
10 A Yes.
11 Q Now, you were asked the contents of
12 Claim 1 whether there were two steps to that
13 claim.
14 Do you recall that?
15 A Yes. I recall that.
16 MR. RATLIFF: Objection. Leading.
17 Q Does the claim itself explain what those
18 two steps are intended to achieve?
19 MR. RATLIFF: Objection. Form.
20 A Yes.
21 Q What is that?
22 MR. RATLIFF: Objection. Form.

1 A The purpose of the first step is
2 determining that the patients colorectal
3 cancer is a Microsatellite Instability-High
4 or mismatch repair deficient; and the purpose
5 of the second step, which is a response to
6 that determination is to treat the patient
7 with a therapeutically effective amount of
8 pembrolizumab.
9 Q What do the first three lines of the
10 claim tell you as a -- looking through the
11 lens of a person of skill in the art?
12 A It's teaching a person of skill in the
13 art that this is a novel, useful method for
14 treating a subset of colorectal cancer
15 patients.
16 Q Turning your attention to Claim 14.
17 Same basic question. The first here,
18 the first four lines of the claim. What
19 would those teach a person of skill in the
20 art about the purpose of the ensuing two
21 steps?
22 MR. RATLIFF: Objection. Beyond the

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

1 compared to other tumors such as DLBCL,
2 ovarian, GBM, that have higher tumor
3 mutational burden than RCC, but are not
4 sensitive to PD-1 blockade. That hypothesis,
5 it's an interesting hypothesis. That
6 hypothesis is, in fact, what is required for
7 effective immunotherapy is the elicitation of
8 a diverse immune response.
9 And I think that, well, it was an
10 interesting hypothesis at the time, but there
11 was also evidence already at the time that
12 the diverse response was not, in fact,
13 required and I would have started with the
14 preclinical data from Bob Schreiber's lab
15 showing that in a mouse tumor model that
16 there might be one or two dominant antigens
17 that are, in fact, entirely responsible for
18 the immune destruction of tumors. Because
19 deletion of those antigens resulted in tumors
20 that grew out. And then that, I think was
21 translated into the clinic for the work of
22 Toni Ribas and colleagues from UCLA, where

1 they followed the diversification of immune
2 response in patients that are treated with
3 either CTLA-4 blockade or PD-1 blockade. And
4 while they did see an expanding diversity of
5 immune response in CTLA-4 blockade treated
6 patients, they did not see that in the PD-1
7 treated patients.
8 Q Thank you. I'm going to switch gears a
9 bit.
10 You were asked about Exhibit 1053, which
11 was a Bristol Myers Squibb clinical trial
12 posting, do you recall those questions
13 generally?
14 A Yes.
15 Q Now, that clinical trial posting
16 Exhibit 1053, is it your recollection that
17 that was posted in 2014?
18 A That's my recollection, yes.
19 Q When was the JHU clinical trial posting
20 done, and that's Exhibit 1005? Just what
21 year if you recall.
22 A My recollection is 2013, but I don't

1 have that in front of me.
2 MR. RATLIFF: If you're going to help
3 him with that, objection. Leading.
4 MR. MILLER: I am helping him with it
5 exactly as I helped him with it
6 throughout your entire deposition.
7 I'm putting up the document for him to
8 see.
9 A Yes. June 2013, that's -- my
10 recollection was correct.
11 Q Which came first, the Bristol Myers or
12 the Hopkins clinical trial posting?
13 A The Hopkins.
14 Q Did the Bristol Myers posting come after
15 Dr. Pardoll sought support from Bristol Myers
16 for its clinical trial?
17 MR. RATLIFF: Objection. Beyond the
18 scope.
19 A My recollection is the conversations
20 between Hopkins and Bristol Myers began in
21 2012, so a year earlier.
22 Q Did the posting of the JHU clinical

1 trial on clinicaltrials.gov have any
2 influence on BMS's decision to pursue it's
3 own clinical trial?
4 MR. RATLIFF: Objection. Leading.
5 A I don't remember it ever being
6 discussed.
7 Q Did Bristol Myers Squibb publish any
8 results from the clinical trial, Exhibit 1053
9 before the clinical date -- sorry, before the
10 critical date of the '393 patent?
11 MR. RATLIFF: Objection. Beyond the
12 scope.
13 A No.
14 Q Would a person of ordinary skill in the
15 art have known the results of the Bristol
16 Meyers clinical trial before the '393
17 Patent's clinical date?
18 A No. No.
19 Q You were shown at the very end of
20 counsel's examination Exhibit 1120. Which
21 was a press release where the FDA granted
22 accelerated approval for MSI-High indication,

1 do you recall that?
2 A Yes. That was in 2017.
3 Q I was going to ask you what year it was,
4 what year was that in?
5 A 2017.
6 Q It's fair to say that press release,
7 Exhibit 1120, post dates the critical date by
8 two years or thereabouts?
9 A Thereabouts.
10 Q The -- returning to the '393 Patent, you
11 were asked about the citation on the second
12 page?
13 A Yes and I think now I will have an
14 easier time finding the second page. I
15 apologize these pages are unnumbered -- oh,
16 they are numbered now I see.
17 Q If I turn your attention to Pages 2 and
18 3.
19 A Okay.
20 Q Do you see citations to the Bristol
21 Myers clinical trial NCT2060188, which begin
22 mid way in the first column on Page 2?

1 A Yes.
2 Q And go to the end of that first column.
3 A Yes.
4 MR. RATLIFF: Objection. Leading.
5 Q And do the citations to the various
6 versions of clinical trial encompass the
7 entirety of the right hand column of Page 2?
8 A Yes.
9 Q And do the citations to the clinical
10 trial encompass about three-fourths of the
11 left column of Page 3 of the '393 Patent?
12 A That appears to be relatively accurate.
13 Q I believe you testified that in your
14 account there were at least 31 citations to
15 the various versions of that clinical trial?
16 A At least.
17 Q Does that strike you as John Hopkins
18 trying to keep the Bristol Myers clinical
19 trial a secret from the patent office during
20 the prosecution of the '393 Patent clinical
21 patent?
22 A No.

1 Q Do you have any understanding as to who
2 funded the JHU clinical trial, the Phase II
3 clinical trial, that emerged from
4 Exhibit 1005?
5 MR. RATLIFF: Objection. Beyond the
6 scope.
7 A Because my memory I can't place where I
8 formed that opinion from, so I would have to
9 say I don't recall.
10 Q Fair enough.
11 Do you recall whether Dr. Pardoll told
12 you where Hopkins would get funding for to
13 conduct that clinical trial, the Phase II
14 clinical trial, that ensued from
15 Exhibit 1005?
16 A I don't recall a conversation --
17 MR. RATLIFF: Objection. Beyond the
18 scope.
19 Q Do you recall when Dr. Pardoll told you
20 that Merck did not fund the Phase II clinical
21 trial that ensued from Exhibit 1005?
22 MR. RATLIFF: Objection. Leading.

1 Objection. Beyond the scope.
2 A I don't have a recollection of the time.
3 Q Approximately?
4 MR. RATLIFF: Objection. Leading.
5 Objection. Beyond the scope.
6 A No.
7 Q Do you recall whether it was when you
8 were still employed at Bristol Myers?
9 A Yes.
10 MR. RATLIFF: Objection. Form.
11 Q And so while you were employed at
12 Bristol Myers, do you recall Dr. Pardoll
13 telling you that Merck did not fund its
14 clinical trial that ensued from Exhibit 1005?
15 A Yes.
16 MR. MILLER: Objection. Leading.
17 Objection. Beyond the scope.
18 Q When did you stop working at Bristol
19 Myers Squibb?
20 A May 2019.
21 Q That's the hardest question of the day.
22 MR. MILLER: Thank you. That's all

1 the questions I have at this moment.
2 Pass the witness.
3 MR. RATLIFF: Let's take a break.
4 (Whereupon, a recess was taken
5 from 7:13 PM until 7:22 PM.)
6 MR. RATLIFF: Okay. Doctor, I have no
7 further questions for you at this
8 particular time. Thank you for your
9 time. I believe I'll be seeing you
10 again with respect to some other
11 cases, but thank you, and I'd like to
12 also thank the court reporter and the
13 remote tech for their services today.
14 MR. MILLER: Yes, thank you all.
15 Thanks, Preston. Good to meet you.
16 COURT REPORTER: Do you want a copy of
17 the transcript?
18 MR. MILLER: Just the transcript.
19 (Whereupon, this examination was
20 concluded at 7:23 PM.)
21
22

1 _____
2 NILS LONBERG
3
4
5 Subscribed and sworn to
before me on this ____ day
6 of _____, _____.
7
8 _____
Notary Public
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1 I N D E X

2 WITNESS: NILS LONBERG

3 EXAMINATION BY	PAGE
4 MR. RATLIFF	4
5 MR. MILLER	241

6

7 E X H I B I T S

8 EXHIBITS	DESCRIPTION	PAGE
9 Exhibit 2072	Declaration of Dr. Nils Lonberg, dated 10-4-24	9
11 Exhibit 1001	US Patent No. 11,591,393 B2, dated 2-28-23	22
13 Exhibit 1005	Study NCT01876511, dated 6-10-13	90
14 Exhibit Paper 10	Decision Granting Institution of Inter Partes Review, dated 6-13-24	123
17 Exhibit 1007	"Clinical Relevance of Microsatellite Instability in Colorectal Cancer," published 7-10-10	145
20 Exhibit 1010	"Microsatellite Instability Detection by Next Generation Sequencing," published September	157

	2014	
Exhibit 1006	"Colorectal cancer and immunity," published 4-14-14	166
Exhibit 1053	Study NCT02060188, dated 2-10-14	174
Exhibit 1009	"Colon Cancer, Version 3.2014, Clinical Practice Guidelines in Oncology," published July 2014	177
Exhibit 1011	"Safety and Tumor Responses with Lambrolizumab (Anti-PD-1) in Melanoma," published 7-11-13	181
Exhibit 1032	"Exomics and immunogenics: Bridging mutational load and immune checkpoints efficacy," published January 2014	185
Exhibit 1039	Description of presentation "Immune checkpoints expression in MSI versus MSS colorectal cancers and their potential therapeutic implications" on 5-31-14	199
Exhibit 1084	"Caris Life Sciences Research Provides	204

	Key Clinical Insights on Immunotherapeutic Targets in a Broad Range of Cancers," dated 6-10-14	
Exhibit 1120	"FDA grants nivolumab accelerated approval for MSI-H or dMMR colorectal cancer"	238

1 C E R T I F I C A T E
2
3 I, KIARA MILLER,
4 a Shorthand Reporter and Notary Public of the
5 State of New York, do hereby certify:
6
7 That the witness whose examination is
8 hereinbefore set forth, was duly sworn or
9 affirmed by me, and the foregoing transcript is
10 a true record of the testimony given by such
11 witness.
12
13 I further certify that I am not related to any
14 of the parties to this action by blood or
15 marriage, and that I am in no way interested in
16 the outcome of this matter.
17
18 Kiara Miller
19 _____
20 KIARA MILLER
21
22