

1 UNITED STATES PATENT AND TRADEMARK OFFICE

2 -----

3 BEFORE THE PATENT TRIAL AND APPEAL BOARD

4 -----

5 MURRAY & POOLE ENTERPRISES LTD.,

6 Petitioner

7
8 V.

9 INSTITUT DE CARDIOLOGIE DE MONTREAL,

10 Patent Owner.

11 -----

12 Case IPR2023-01064

13 Patent 11,400,063

14 -----

15
16 Videotaped Deposition of HOSSEIN ARDEHALI, M.D.

17 Tuesday, June 18, 2024

18 9:13 a.m. CST

19 Job No.: 540840

20 Pages: 1 - 215

21 Reported Stenographically by:

22 Tiffany M. Pietrzyk, CSR RPR CRR

1 Videotaped deposition of HOSSEIN ARDEHALI, M.D.,
2 held at the location of:

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12

13 Pursuant to notice, before Tiffany M. Pietrzyk, a
14 Certified Shorthand Reporter in the States of
15 Illinois, Texas, and California, Registered
16 Professional Reporter, Certified Realtime Reporter,
17 and a Notary Public in and for the State of
18 Illinois.
19
20
21
22

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E X H I B I T S

(Retained by counsel.)

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Transcript of Hossein Ardehali, M.D.
Conducted on June 18, 2024

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iron alleviates cardiac	
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O'Keefe, et al. Entitled,	
"Ineffectiveness of	
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Exhibit 2010 Article entitled, "High 136
versus low dosing of oral
colchicine for early acute
gout flare," by Terkeltaub,
et al.

Exhibit 2054 Paper authored by Nina 168
Raju, et al., entitled,
"Effect of colchicine
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1	P R O C E E D I N G S	09:10:24
2	THE VIDEOGRAPHER: Good morning.	09:13:04
3	Here begins Media Number 1 in the videotaped	09:13:05
4	deposition of Dr. Hossein Ardehali, in the matter of	09:13:08
5	Murray & Poole Enterprises, Ltd. vs. Institut de	09:13:14
6	Cardiologie de Montreal (PTAB), filed in the United	09:13:23
7	States Patent Trademark Office before the Patent	09:13:27
8	Trial and Appeals, Case Number IPR2023-01064.	09:13:30
9	Today's date is June 18, 2024. The time on	09:13:39
10	the video monitor is now 9:13 a.m.	09:13:44
11	The videographer today is Cary Davidow,	09:13:52
12	representing Planet Depos.	09:13:54
13	This video deposition is taking place at	09:13:55
14	233 South Wacker Drive, Suite 7100, Chicago,	09:13:57
15	Illinois.	09:14:00
16	Would counsel please voice identify	09:14:00
17	themselves and state whom they represent.	09:14:02
18	MR. LAURENCE: Kevin Laurence of Laurence &	09:14:04
19	Phillips IP Law. And to my right is Joanna Brougher	09:14:06
20	of BioPharma Law Group, and remotely is Tom Siepmann	09:14:10
21	of BioPharma Law Group and Matt Phillips of	09:14:15
22	Laurence & Phillips IP Law.	09:14:19

Transcript of Hossein Ardehali, M.D.
Conducted on June 18, 2024

11

1	MR. WILKERSON: Matthew Wilkerson of	09:14:21
2	ArentFox Schiff, on behalf of the witness as well as	09:14:25
3	the patent owner. And with me remotely is Sailesh	09:14:29
4	Patel of the same firm, as well as some of our	09:14:34
5	summer associates of ArentFox Schiff, Bella Santos,	09:14:37
6	Jacob Blaise, and Grant Everly.	09:14:42
7	THE VIDEOGRAPHER: The court reporter today	09:14:47
8	is Tiffany Pietrzyk, representing Planet Depos.	09:14:48
9	The witness will now be sworn.	09:14:50
10	(Witness sworn.)	09:15:09
11	MR. LAURENCE: If we could pause for a	09:15:09
12	moment, there's a technical problem.	09:15:10
13	THE VIDEOGRAPHER: Going off the record at	09:15:12
14	9:14 a.m.	09:15:14
15	(A short break was had.)	09:15:15
16	THE VIDEOGRAPHER: Going back on the record	09:16:14
17	at 9:15 a.m.	09:16:16
18	///	
19	///	
20	///	
21	///	
22	///	

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IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1076

1 WHEREUPON:

09:16:16

2 HOSSEIN ARDEHALI, M.D.,

09:16:16

3 called as a witness herein, having been first duly

09:16:16

4 sworn, was examined and testified as follows:

09:16:16

5 EXAMINATION

09:16:18

6 BY MR. LAURENCE:

09:16:18

7 Q. Dr. Ardehali, you've been placed under oath.

09:16:21

8 You must give truthful and complete answers. You're

09:16:23

9 testifying under penalty of perjury laws of the

09:16:26

10 United States.

09:16:28

11 Tell me if questions are not clear and

09:16:29

12 understandable. And if you answer my question, I'll

09:16:32

13 assume you understood it.

09:16:34

14 Is it okay if I refer to the patent owner as

09:16:37

15 MHI?

09:16:41

16 A. Sure.

09:16:42

17 Q. So MHI's counsel will have the right to make

09:16:42

18 objections for the record, but you must still answer

09:16:46

19 unless instructed not to.

09:16:49

20 And Tiffany Pietrzyk is a certified

09:16:52

21 shorthand reporter. She will take down everything

09:16:57

22 said on the record and later make a transcript.

09:17:00

1	Then after the transcript is created, we'll forward	09:17:01
2	that to you. You need to review it and see if there	09:17:03
3	are any errors. And if there are, note those and	09:17:07
4	then sign the transcript so that we can file that as	09:17:11
5	an exhibit.	09:17:15
6	A. Okay.	09:17:15
7	Q. And we must speak audibly and clearly. For	09:17:16
8	example, please answer yes or no instead of moving	09:17:27
9	your head or saying "yeah." And only one person can	09:17:29
10	speak at a time.	09:17:32
11	So if you could state your full name for the	09:17:34
12	record?	09:17:38
13	A. Sure. First name is H-o-s-s-e-i-n, last	09:17:38
14	name is A-r-d-e-h-a-l-i. So it's Hossein Ardehali.	09:17:44
15	Q. And have you ever had or used any other name	09:17:50
16	in the U.S.?	09:17:53
17	A. No.	09:17:53
18	Q. And what is your address?	09:17:54
19	A. My home address?	09:17:54
20	Q. Yes.	09:17:55
21	A. 1259 West Wrightwood Avenue, with a W,	09:17:56
22	Chicago, Illinois 60614.	09:18:00

1	Q. And is there any reason you cannot	09:18:03
2	competently testify today? Any mental or physical	09:18:05
3	condition, medication, drugs, alcohol, or anything	09:18:09
4	else that might impair your ability to testify?	09:18:11
5	A. No.	09:18:13
6	Q. Have you ever served as an expert in other	09:18:13
7	patent cases?	09:18:16
8	A. Yes.	09:18:17
9	Q. What was the case?	09:18:17
10	A. Oh, there was one case on cangrelor. There	09:18:19
11	was, I think, another one on the brand name for	09:18:26
12	dofetilide. And there were, I think, a couple of	09:18:29
13	more cases. I can't remember.	09:18:39
14	Q. Were those in district court, or were they	09:18:41
15	at the patent office?	09:18:43
16	A. No. They were in district court.	09:18:45
17	Q. And what was the scientific topic of the	09:18:46
18	cases?	09:18:52
19	A. Again, I can't remember all the details, but	09:18:54
20	with cangrelor, I believe it was related to the	09:18:58
21	generic versus brand name. And I think the other	09:19:01
22	ones were related to the same issue.	09:19:05

1	Q. Is that -- and Sanofi V Glenmark, is that	09:19:10
2	the case?	09:19:13
3	A. I think, yes, that was with Sanofi, yes.	09:19:14
4	Q. And were you deposed in that case?	09:19:16
5	A. Yes, I was.	09:19:19
6	Q. How many times have you been deposed?	09:19:20
7	A. In general?	09:19:22
8	Q. Uh-huh.	09:19:22
9	A. I would say probably 30 times.	09:19:23
10	Q. And how many of those were patent cases or	09:19:26
11	related to patents?	09:19:28
12	A. Five or six.	09:19:29
13	Q. Okay. And do you understand that you may be	09:19:34
14	deposed today for up to seven hours on the record?	09:19:42
15	A. Yes.	09:19:45
16	Q. Okay. So what degrees do you have?	09:19:45
17	A. I have an M.D., a Ph.D., I have a bachelor's	09:19:49
18	degree, and a high school diploma, so that one comes	09:19:53
19	last, yeah.	09:19:59
20	Q. Okay. And what was your undergraduate	09:19:59
21	degree in?	09:20:02
22	A. Computer science.	09:20:03

1	Q. And then your Ph.D.?	09:20:04
2	A. In the department of molecular physiology	09:20:05
3	and biophysics.	09:20:10
4	Q. So have you ever been called a polymath?	09:20:11
5	A. No. First time I've heard that.	09:20:14
6	Q. Well, you deserve it. That's an impressive	09:20:16
7	background.	09:20:20
8	A. Thank you.	09:20:20
9	Q. What is your background in statistics?	09:20:21
10	A. I took a statistics class when I was	09:20:26
11	undergrad at the University of Utah. That's the	09:20:29
12	extent of what I know about statistics. And in	09:20:34
13	addition to that, we use statistics in our research.	09:20:37
14	Q. Uh-huh.	09:20:40
15	A. So we use it on a daily basis.	09:20:41
16	Q. So have you published anything where you	09:20:43
17	required the use of a biostatistician?	09:20:47
18	A. Well, we use the statistics in our analysis	09:20:53
19	but in terms of using a biostatistician, we are	09:20:56
20	doing a clinical study, and we use the	09:20:59
21	biostatistician to help us with power calculation.	09:21:02
22	Q. Okay. Would you consider yourself not to be	09:21:05

1 an expert in statistics?

09:21:13

2 A. I have some expertise in statistics. Basic
3 expertise, but in terms of complicated questions
4 related to statistics, I agree with that. I think
5 that's a fair statement.

09:21:15

09:21:20

09:21:22

09:21:25

6 Q. Okay. Could you describe your areas of
7 research, to the extent it's publicly available,
8 that you've done over the last three years or so?

09:21:25

09:21:30

09:21:37

9 A. Sure. So my research is mostly basic
10 science. And I work -- half of my lab work is on
11 the role of iron and cardiovascular disease, and the
12 other half of my lab work is on metabolism. And we
13 are specifically interested in the role of glucose
14 metabolism, hexokinases in immune cells, in
15 inflammation, and how it relates to cardiovascular
16 disease and cancer.

09:21:39

09:21:43

09:21:45

09:21:48

09:21:53

09:21:55

09:22:00

09:22:04

17 We are also doing some clinical studies.
18 I'm helping with those studies, and I'm serving as a
19 co-investigator in some of those studies.

09:22:05

09:22:08

09:22:11

20 But yeah, so that's basically the extent of
21 my research.

09:22:14

09:22:18

22 Q. And going back further, say, three to ten

09:22:19

1	years back, similar focus or different?	09:22:23
2	A. No. It was very similar, yes.	09:22:26
3	Q. So you've focused on the same areas in	09:22:28
4	general since you've been a doctor?	09:22:31
5	A. Yes.	09:22:33
6	Q. Have you run any clinical trials?	09:22:33
7	A. Well, we are doing a Phase 2 clinical trial,	09:22:42
8	and I initiated the study, but somebody else is	09:22:44
9	doing it. We are trying to submit an R01.	09:22:50
10	Actually, right before this session, I got an email	09:22:53
11	on the submission of the R01. R01 refers to a big	09:22:55
12	grant from the NIH, so we are trying to get the	09:22:59
13	funding for that. And, again, I serve as a	09:23:02
14	co-investigator because now somebody else -- I gave	09:23:06
15	it to somebody else to run it.	09:23:08
16	Q. Based on your research, does that require	09:23:09
17	you to understand how the FDA works?	09:23:12
18	A. Yeah. In general terms, yes.	09:23:16
19	Q. And you may have answered this already, but	09:23:18
20	have you been a principal investigator?	09:23:23
21	A. On several grants, yes.	09:23:26
22	Q. Yeah?	09:23:28

1	A. Yes.	09:23:29
2	Q. Are you an inventor on my patents?	09:23:29
3	A. I have a number of patents, yes.	09:23:37
4	Q. Any ballpark idea of how many?	09:23:39
5	A. I think I have four or five, yeah.	09:23:40
6	Q. Do you have any pending applications?	09:23:42
7	A. There is one that I think just got	09:23:47
8	submitted, so I don't know what the status is, yeah.	09:23:49
9	Q. Okay.	09:23:53
10	I'm handing you a copy of Exhibit 1058.	09:24:12
11	(Exhibit 1058 was marked for	09:24:17
12	identification and was retained by counsel.)	09:24:21
13	Q. Which is --	09:24:21
14	THE VIDEOGRAPHER: Counsel, microphone.	09:24:24
15	BY MR. LAURENCE:	09:24:48
16	Q. Are you familiar with U.S. Patent	09:24:49
17	10,258,612?	09:24:51
18	THE VIDEOGRAPHER: Counsel, I can't hear	09:24:59
19	you.	09:25:01
20	BY MR. LAURENCE:	09:25:11
21	Q. Are you familiar with U.S. patent	09:25:12
22	10,258,612?	09:25:14

1	A. Yes. I know this was filed. The lawyers	09:25:17
2	sent me the electronic copy. It's somewhere in my,	09:25:19
3	you know, computer, but this is the first time I've	09:25:21
4	actually seen the hard copy, yes.	09:25:23
5	Q. Do you mind if I refer to it as the Ardehali	09:25:25
6	patent?	09:25:28
7	A. Sure.	09:25:28
8	Q. Was the technology in the Ardehali patent	09:25:29
9	commercialized?	09:25:33
10	A. Not yet, no.	09:25:35
11	Q. How many professional publications do you	09:25:36
12	have?	09:25:44
13	A. I think right now. Probably close to 120.	09:25:44
14	Q. Do any of them concern post hoc analyses of	09:25:48
15	completed studies?	09:25:53
16	A. Not that I can think of right now.	09:25:58
17	Q. Do any of them analyze timing of treatment?	09:26:02
18	A. Not in patients, no.	09:26:11
19	Q. And do any of them analyze time-to-trial	09:26:13
20	initiation?	09:26:16
21	A. No.	09:26:19
22	Q. And what is your relationship with MHI?	09:26:20

1	A. MHI is the Montreal Health Institute. I	09:26:27
2	have no relationship with them.	09:26:32
3	Q. Other than as an expert witness?	09:26:35
4	A. Correct.	09:26:37
5	Q. And what is your relationship with	09:26:38
6	Pharmascience?	09:26:42
7	A. I don't have a relationship with them.	09:26:42
8	Q. Okay. Other than also as an expert witness	09:26:43
9	for them?	09:26:47
10	A. Yes.	09:26:47
11	Q. And what is your relationship with	09:26:48
12	Pendopharm?	09:26:50
13	A. I don't know who they are.	09:26:51
14	Q. Do you have a contract with any of these	09:26:52
15	organizations?	09:26:56
16	A. Not that I know of.	09:26:58
17	Q. So your only relationship is in the role as	09:26:59
18	an expert witness; is that correct?	09:27:05
19	A. I believe so, yes.	09:27:07
20	Q. And how were you contacted to become an	09:27:08
21	expert in this case?	09:27:22
22	A. I can't remember. I believe there was an	09:27:22

1	email that was sent to me.	09:27:23
2	Q. Have you published any articles related to	09:27:25
3	colchicine?	09:27:34
4	A. Not directly, no.	09:27:36
5	Q. When did you become aware of trials	09:27:37
6	involving colchicine?	09:27:43
7	Not trials in the litigation sense, but in	09:27:44
8	the regulatory sense?	09:27:47
9	A. Well, I knew there were studies on	09:27:49
10	colchicine in pericarditis, and I knew that there	09:27:52
11	were studies going on on colchicine related to its	09:27:57
12	effects on -- or its anti-inflammatory effects and	09:28:01
13	its role in cardiovascular disease.	09:28:04
14	Q. Do you know about when you became aware of	09:28:13
15	those trials?	09:28:15
16	A. I would say many years ago.	09:28:17
17	Q. What are some side effects of colchicine?	09:28:19
18	A. I know that it can have GI side effects.	09:28:27
19	That's what we tell our patients, that there is a	09:28:31
20	risk of GI side effects. That's the major side	09:28:35
21	effect we have seen with colchicine, diarrhea	09:28:38
22	sometimes constipation GI -- you know, indigestion	09:28:41

1 or gastroesophageal reflux disease. We haven't seen 09:28:45
2 as much infectious -- you know, opportunistic 09:28:51
3 infections with colchicine. But potentially, you 09:28:55
4 can -- you know, your immune system can go down and 09:28:58
5 you can have additional infections. But the drug is 09:29:01
6 relatively safe. 09:29:04

7 Q. Is fatigue another side effect? 09:29:14

8 A. It could be. Again, I can't remember all 09:29:16
9 the side effects, but it could be. 09:29:19

10 Q. And are those side effects that occur when 09:29:22
11 taken as prescribed? 09:29:26

12 A. Yes, they can happen, yes. 09:29:30

13 Q. And what would be a side effect if you were 09:29:32
14 to take colchicine in larger doses than prescribed? 09:29:35

15 MR. WILKERSON: Objection to form. 09:29:39

16 A. Again, I think the GI side effects can be 09:29:41
17 exacerbated. And in terms of additional side 09:29:44
18 effects, again, I can't remember all the additional 09:29:49
19 side effects. 09:29:52

20 Q. And what is a safe amount of colchicine to 09:29:53
21 be taken on a daily basis? 09:29:57

22 A. Well -- 09:30:00

1	MR. WILKERSON: Objection. Form.	09:30:00
2	A. -- the dosage we have available in this	09:30:01
3	country is .6 milligrams. So in Europe, it's	09:30:04
4	.5 milligrams. In our patients with pericarditis,	09:30:09
5	we usually give them a loading dose, so it's usually	09:30:14
6	1.2 milligram loading dose, sometimes even higher.	09:30:18
7	And depending on how they tolerate, we maintain them	09:30:21
8	on .6 milligrams after the loading dose.	09:30:25
9	Q. Why do you give a loading dose with	09:30:28
10	pericarditis?	09:30:30
11	A. When?	09:30:31
12	Q. Why?	09:30:32
13	A. So the idea here is to attack inflammation	09:30:33
14	as effectively as possible. So the idea is to give	09:30:37
15	a loading dose to make sure that the inflammation is	09:30:40
16	under control and then maintain it with a	09:30:44
17	maintenance dose.	09:30:47
18	Q. Okay. And what would -- what is your view	09:30:50
19	of a dose of 1.2 milligrams? Would that be safe?	09:30:55
20	MR. WILKERSON: Objection. Form.	09:30:59
21	A. So you are asking if 1.2 --	09:31:01
22	Q. On a daily basis?	09:31:03

1	A. So you're asking if 1.2 milligram daily dose	09:31:05
2	is a safe dose. Again, that's relative term,	09:31:08
3	"safety." I would say that 1.2 milligrams per day	09:31:13
4	can be a safe dose in a lot of patients.	09:31:17
5	Q. And would that be true for gout treatment?	09:31:20
6	A. 1.2 milligrams?	09:31:23
7	Right, so in terms of gout, we also usually	09:31:25
8	give a loading dose. And 1.2 milligram daily dose	09:31:28
9	is what we start with, and many of our patients can	09:31:32
10	tolerate that.	09:31:36
11	Q. And with gout, are you doing a loading dose	09:31:38
12	because a patient has an onset of pain and it needs	09:31:42
13	to be dealt with?	09:31:45
14	MR. WILKERSON: Objection. Form.	09:31:47
15	A. Well, again, the idea is not just pain. The	09:31:48
16	idea here is that there is an inflammatory process	09:31:51
17	going on in the patient and gout is -- I'm sorry --	09:31:55
18	colchicine is given to patients to target that, you	09:32:00
19	know, acute inflammatory process as effectively as	09:32:03
20	possible.	09:32:08
21	Q. And what differences for treatment of gout	09:32:10
22	as a cardiologist would you give?	09:32:20

1	A. I'm sorry. Can you repeat the question?	09:32:27
2	Q. Sorry.	09:32:29
3	For treatment of gout, as a cardiologist,	09:32:32
4	what is the amount that you would prescribe?	09:32:35
5	MR. WILKERSON: Objection. Form.	09:32:38
6	A. Right. So as a cardiologist, we don't	09:32:39
7	generally treat gout. There are patients who come	09:32:43
8	to us who have already been started on colchicine by	09:32:45
9	their primary care physician, and so we are familiar	09:32:49
10	with the treatment of gout, but we are not generally	09:32:53
11	the physicians who start colchicine for those	09:32:57
12	patients. But, again, in those patients, because of	09:32:59
13	the acute inflammatory process, they are usually	09:33:02
14	given a loading dose.	09:33:07
15	Q. And so what -- as a cardiologist, what ways	09:33:08
16	do you use colchicine?	09:33:13
17	A. So we use colchicine in pericarditis. And,	09:33:17
18	you know, soon we may use it in patients with	09:33:21
19	cardiovascular disease. And there are some patients	09:33:24
20	with familial Mediterranean fever who may come to	09:33:27
21	us. I've had one or two in my lifetime, but they	09:33:32
22	are usually referred to primary care physicians for	09:33:38

1 their management.

09:33:40

2 Q. And for pericarditis, what's a typical
3 dosage that you prescribe?

09:33:42

09:33:45

4 A. Right. So I teach my interns, my medical
5 students, my fellows that they should be started on
6 loading dose. Usually, we go for seven to ten days,
7 sometimes three months of a loading dose, and then
8 we go to maintenance dose.

09:33:46

09:33:49

09:33:55

09:34:01

09:34:04

9 Q. And why do you give a loading dose with
10 pericarditis?

09:34:06

09:34:08

11 A. Right. So the idea here is to reduce the
12 inflammatory process. Pericarditis can be a severe
13 inflammatory process. And if the pericardial sack
14 becomes thickened because of that inflammatory
15 process, it can cause chronic pericarditis, and it
16 can lead to chronic pericardial effusion. So the
17 idea is to reduce inflammation as much as possible
18 at the beginning and maintain those patients on a
19 maintenance dose.

09:34:08

09:34:10

09:34:16

09:34:20

09:34:24

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09:34:32

09:34:36

09:34:38

20 Q. When you say that pericarditis is chronic,
21 what do you mean?

09:34:39

09:34:41

22 A. Well, I didn't say pericarditis is chronic.

09:34:42

1 I said it can turn into a chronic condition, so that
2 means the inflammation can continue and go on for a
3 long time. Or the inflammatory process can cause
4 the sack to become thickened -- the sack meaning to
5 the pericardial sack to become thickened, and that
6 can cause an effect on cardiac function and can
7 cause symptoms in patients.

8 Q. You mentioned that you may be using
9 colchicine to treat cardiovascular disease.

10 Has the FDA approved colchicine for
11 cardiovascular disease yet?

12 A. No.

13 Q. Is it fair to say that Dr. Tardif and
14 Dr. Ridker's research is focused more extensively on
15 colchicine than your research?

16 MR. WILKERSON: Objection. Form.

17 A. I don't know if I would characterize it that
18 way. I work on the basic science of inflammation.
19 We work extensively on innate immunity and the role
20 of myeloid cells in inflammation. We study the
21 function of myeloid cells at the basic level, and we
22 study how metabolism affects myeloid cells. So my

1 research is directly related to inflammation and
2 immune cells.

3 Now, colchicine has an effect on immune
4 cells. So in terms of whether or not, you know,
5 they do more research related to colchicine, I would
6 say Dr. Tardif, yes. I know that Dr. Ridker has
7 been doing a lot in terms of inflammation and the
8 role of inflammation in cardiovascular disease.

9 Q. Do you have any professional certifications
10 or licenses?

11 A. Yes, I do.

12 Q. Can you tell us what they are?

13 A. Sure. I'm certified in the -- or I have
14 license in the State of Illinois to practice
15 cardiovascular disease medicine, and I also -- I'm
16 board-certified in cardiology. I have to get my
17 recertification this year, so I'm not looking
18 forward to it.

19 Q. So to be board-certified as a cardiologist,
20 you have to do that process how frequently, in terms
21 of recertifying?

22 A. Right. So recertification is every ten

1 years. American Board of Internal Medicine just 09:37:12
2 changed their policy. So now every year, we can 09:37:14
3 take an exam, and we would be board-certified on a 09:37:18
4 continuous basis. So I'm gonna actually do that 09:37:22
5 starting this year. 09:37:25

6 Q. I'm going to hand you a copy of both of your 09:37:26
7 declarations. 09:37:34

8 MR. WILKERSON: Counsel, if helpful, I can 09:37:38
9 also represent he has a clean copy of each 09:37:40
10 declaration in front of him -- 09:37:42

11 MR. LAURENCE: Okay. 09:37:43

12 MR. WILKERSON: -- that he brought in. If 09:37:44
13 you want to save paper. 09:37:48

14 Thank you. 09:37:51

15 MR. LAURENCE: If I could, I'd like to get 09:37:51
16 the copies back that are clean. 09:37:53

17 BY MR. LAURENCE: 09:38:05

18 Q. Okay. So the thick one is your first 09:38:10
19 declaration. That's Exhibit 2001. 09:38:11

20 (Exhibit 2001 was marked for 09:38:11
21 identification and was retained by counsel.) 09:38:22

22 Q. If you could go to page 4. 09:38:22

1	A. Okay.	09:38:24
2	Q. Paragraph 12.	09:38:25
3	A. Yes.	09:38:28
4	Q. You indicate that you disagree with	09:38:28
5	Dr. Ridker's definition of a person of ordinary	09:38:31
6	skill in the art.	09:38:34
7	Do you see that?	09:38:34
8	A. Yes.	09:38:34
9	Q. And why do you think a person of ordinary	09:38:35
10	skill in the art need not have been aware of	09:38:40
11	research relating to cardiovascular disease	09:38:42
12	progression, including the role of inflammatory	09:38:44
13	pathways in secondary cardiovascular events?	09:38:47
14	A. So I think a person with three to five years	09:38:54
15	of experience in cardiovascular disease would be --	09:38:57
16	would have a general knowledge of this -- of this	09:39:00
17	term and this process. So I don't think they need	09:39:02
18	to know all the details related to the role of the	09:39:05
19	inflammation in cardiovascular disease and secondary	09:39:08
20	prevention.	09:39:13
21	Q. Would it be helpful to understand those?	09:39:14
22	A. Yes.	09:39:18

1	Q. And how were your declarations prepared?	09:39:18
2	A. I can't remember the details, but counsel	09:39:28
3	and I wrote it together, and it went through several	09:39:32
4	revision processes.	09:39:36
5	Q. And who did you work with?	09:39:38
6	A. Mr. Wilkerson.	09:39:39
7	Q. And when was that?	09:39:43
8	A. I don't remember the exact date.	09:39:44
9	Q. Do you recall how much time you spent in	09:39:50
10	preparing the declaration, how many hours?	09:39:52
11	A. No, I don't. Sorry.	09:39:55
12	Q. Ballpark?	09:39:57
13	A. Maybe 15 hours.	09:39:58
14	Q. Okay.	09:40:01
15	A. 15, 20 hours.	09:40:02
16	Q. There was more than one draft?	09:40:05
17	A. I believe so, yes.	09:40:07
18	Q. Have you discussed the content of your	09:40:08
19	declaration with anyone else?	09:40:13
20	A. Besides counsel?	09:40:15
21	Q. Besides Mr. Wilkerson?	09:40:16
22	A. No. Well, there may have been other people	09:40:19

1	cc'd on those emails, but I assume they were lawyers	09:40:22
2	so ...	09:40:25
3	Q. What documents did you read to prepare for	09:40:26
4	writing your declaration?	09:40:33
5	A. Most of them are cited in my declaration,	09:40:37
6	but I read the patent, I read some of the studies	09:40:41
7	that were published in this area. And I read	09:40:48
8	Dr. Ridker's declaration. I guess, you know, I read	09:40:53
9	the provisional patent or provisional submission.	09:41:03
10	And I also read the petitioner's filing. I don't	09:41:07
11	know if I'm using the right terms.	09:41:14
12	Q. Petition?	09:41:16
13	A. Yeah, the petition, yes.	09:41:16
14	Q. Are you aware of any mistakes or	09:41:18
15	inaccuracies in either of your declarations that	09:41:22
16	you'd like to bring to our attention?	09:41:24
17	A. Not -- not that I can think of at this	09:41:27
18	point, no.	09:41:31
19	Q. And what did you do to prepare for this	09:41:31
20	deposition?	09:41:37
21	A. So over the weekend, I reviewed some of the	09:41:38
22	documents and I met with counsel yesterday.	09:41:40

1	Q. How much time did you spend yesterday?	09:41:43
2	A. With counsel? We started at 8 and we were	09:41:47
3	finished close to 5, 4:30, 5, yeah.	09:41:53
4	Q. And did you review any documents to prepare	09:41:56
5	for this deposition that you didn't just refer to as	09:42:00
6	the list of documents you reviewed to prepare your	09:42:05
7	declaration?	09:42:09
8	MR. WILKERSON: I'll just caution you, you	09:42:10
9	can answer, but just don't reveal the substance of	09:42:13
10	any of our communications.	09:42:15
11	A. Not that I can think of, no.	09:42:18
12	Q. When did you first learn about the -- about	09:42:26
13	U.S. Patent Number 11,400,063 that's owned by MHI	09:42:32
14	and is the subject of this IPR?	09:42:41
15	A. When I got involved in this case.	09:42:43
16	Q. Are you okay if I refer to it as the '063	09:42:46
17	patent?	09:42:49
18	A. Yes.	09:42:50
19	Q. Do you have enough familiarity with the	09:42:50
20	claims to answer questions about the claims --	09:42:58
21	A. I believe so, yes.	09:43:01
22	Q. -- on the '063?	09:43:02

1	In Claim 1, what does it mean when it says	09:43:06
2	"low dose"?	09:43:09
3	A. Low dose refers to a dose that is generally	09:43:10
4	as .5 milligrams per day in other countries and	09:43:15
5	.6 milligrams per day generally in North America.	09:43:22
6	Q. What about other countries, what would it	09:43:26
7	mean?	09:43:29
8	A. .5 milligrams per day.	09:43:29
9	Q. You said that you had studied a provisional.	09:43:31
10	You're aware that there are two provisionals;	09:43:43
11	correct?	09:43:46
12	A. Right. There is, if I am not mistaken,	09:43:46
13	there is an '865 and there is one more, '285, if I'm	09:43:49
14	not mistaken.	09:43:53
15	Q. So you've read the '865 provisional?	09:43:55
16	A. Yes.	09:44:00
17	Q. And do you understand it?	09:44:00
18	A. Most of it, yes.	09:44:01
19	Q. And do you agree that the '865 provisional	09:44:02
20	discloses administering colchicine within about	09:44:06
21	30 days of the myocardial infarction at -- let me	09:44:09
22	get a copy of that.	09:44:15

1	MS. BROUGHER: Which one?	09:44:17
2	MR. LAURENCE: Exhibit 1004.	09:44:17
3	(Exhibit 1004 was marked for	09:44:24
4	identification and was retained by counsel.)	09:44:37
5	THE WITNESS: Thank you.	09:44:37
6	BY MR. LAURENCE:	09:44:41
7	Q. So on page 2 of the '865 provisional, and on	09:44:42
8	line 32, do you see where it says, [As read] The	09:44:53
9	method involves administering colchicine within 5,	09:44:56
10	10, 15, 20, or 25 days of the MI?	09:45:00
11	A. Yes.	09:45:03
12	Q. Which of those -- excuse me. Let me take	09:45:03
13	that -- get the patents.	09:45:10
14	MR. LAURENCE: Exhibit 1.	09:45:18
15	(Exhibit 1001 was marked for	09:45:28
16	identification and was retained by counsel.)	09:45:30
17	MR. LAURENCE: I'm handing you a copy of	09:45:30
18	Exhibit 1001, which is the '063 patent.	09:45:34
19	Q. And if you could flip to, towards the end of	09:45:46
20	the patent, in column 41?	09:45:50
21	A. Yes.	09:45:55
22	Q. There's Claim 1?	09:45:56

1	A. Yes.	09:45:57
2	Q. Claim 1 recites, [As read] Initiating the	09:45:57
3	administration of colchicine at a daily low dose to	09:46:04
4	the patient within about three days of the MI.	09:46:07
5	Do you see that?	09:46:10
6	A. No. Can you tell me where?	09:46:10
7	Q. Right in the middle of the page --	09:46:13
8	A. Yeah.	09:46:15
9	Q. -- there's a listing of the claims?	09:46:16
10	A. Yes.	09:46:18
11	Q. And there's Claim 1?	09:46:19
12	A. Yes.	09:46:20
13	Q. And about midway into Claim 1, there's a	09:46:20
14	clause that starts "initiating" in the second line?	09:46:25
15	A. Yes.	09:46:30
16	Q. [As read] Initiating the administration of	09:46:30
17	colchicine at a daily low dose to the patient within	09:46:33
18	about three days of the MI.	09:46:36
19	Do you see that?	09:46:37
20	A. Yes.	09:46:38
21	Q. So in the provisional '865, there on page 2,	09:46:38
22	line 32, it says, [As read] The method involves	09:46:55

1	administering colchicine within 5, 10, 15, 20, or	09:46:58
2	25 days of the MI.	09:47:03
3	Which of those end points provides support	09:47:07
4	for claiming, in the '063 patent, Claim 1, within	09:47:10
5	three days of the myocardial infarction?	09:47:16
6	MR. WILKERSON: Objection. Form.	09:47:19
7	A. So if I understand your question correctly,	09:47:20
8	you're asking me, in terms of time frame of three	09:47:23
9	days, which element of statement on line 30 --	09:47:27
10	Q. 32.	09:47:33
11	A. -- 32 correlates with what is in the '063?	09:47:33
12	Q. Correct.	09:47:40
13	A. So the answer to that question is that	09:47:41
14	within five days fully captures within three days.	09:47:43
15	Q. Okay. And does 10 days also cover that?	09:47:46
16	A. So three days, yes. In terms of math, yes,	09:47:49
17	three days is within 10 days, but it is a longer	09:47:54
18	period compared to five days.	09:47:56
19	Q. Understood. And is the same true for	09:47:58
20	15 days?	09:48:01
21	A. Yes.	09:48:01
22	Q. And 20 days?	09:48:02

1	A. Right. Again, in terms of the length, it's	09:48:03
2	longer, but three days is fully captured in those	09:48:06
3	time frames.	09:48:11
4	Q. Okay. And 25 days?	09:48:12
5	A. Yes.	09:48:14
6	Q. Then, in line 36, it says, [As read] The	09:48:14
7	method includes administering colchicine at about	09:48:19
8	30 days.	09:48:22
9	Would the same -- I'm sorry. In the '865	09:48:24
10	provisional, page 2, line 36.	09:48:29
11	A. Okay.	09:48:31
12	Q. It says -- starting at line 35, actually --	09:48:31
13	[As read] The method includes administering	09:48:36
14	colchicine at about 30 days of the myocardial	09:48:39
15	infarction.	09:48:42
16	Would the same be true for 30 days?	09:48:42
17	MR. WILKERSON: Objection. Form.	09:48:45
18	A. Well, again, it's a longer time, but the	09:48:45
19	three days falls within 30 days.	09:48:48
20	Q. Going back to the claims in the '063 patent,	09:48:57
21	in Claim 28, do you see that in column 42?	09:49:17
22	A. Yes.	09:49:21

1	Q. It recites, [As read] Administering	09:49:21
2	colchicine within 4 to 7 days of the MI.	09:49:24
3	Is it fair to say that all of the same	09:49:28
4	listed number of days in the '865 provisional	09:49:33
5	provides support for this range of 4 to 7 days?	09:49:41
6	A. Again, I agree that, in terms of math,	09:49:46
7	within 4 to 7 days falls within 30 days.	09:49:49
8	Q. In your second declaration at paragraph 21,	09:50:27
9	you state that, [As read] A POSA -- which is the	09:50:55
10	acronym for a person of ordinary skill in the art --	09:50:57
11	would understand that the language "within 4 to	09:51:00
12	7 days of the MI" to mean that the colchicine should	09:51:03
13	be initiated on the first, second, third, fourth,	09:51:05
14	fifth, sixth or seventh day after an MI.	09:51:09
15	Can you point to anything in the '865	09:51:16
16	provisional that supports initiating on the first,	09:51:19
17	second, or third day?	09:51:26
18	A. I'm sorry. Did you -- can you repeat that?	09:51:28
19	I don't think I followed you.	09:51:31
20	Q. Okay. So I'm referring to your second --	09:51:33
21	A. Yes.	09:51:39
22	Q. -- declaration, which is Exhibit 2072.	09:51:39

1	(Exhibit 2072 was marked for	09:51:39
2	identification and was retained by counsel.)	09:51:45
3	A. Yes.	09:51:45
4	Q. And in paragraph 21, starting in the first	09:51:45
5	line.	09:51:49
6	A. Yes.	09:51:50
7	Q. You state, [As read] A POSA --	09:51:50
8	A. Yes.	09:51:52
9	Q. -- would understand that the language of	09:51:52
10	"within about 3 days of the MI" to mean that the	09:51:54
11	colchicine should be initiated on the first, second,	09:51:57
12	or third day after an MI.	09:52:00
13	Then the next sentence, [As read] Similarly,	09:52:05
14	a POSA would understand that the language "within 4	09:52:08
15	to 7 days of the MI" to mean that the colchicine	09:52:11
16	should be initiated on the first, second, third,	09:52:14
17	fourth, fifth, sixth, or seventh day after an MI.	09:52:16
18	And my question is, what basis can you point	09:52:21
19	to for initiating on the first, second, or third day	09:52:23
20	for the 4-to-7-day range?	09:52:26
21	MR. WILKERSON: Objection to form.	09:52:37
22	A. Yeah, I'm still not clear. You're saying	09:52:38

1 within 4 to 7 days, why would it refer to first,
2 second, and third day?

3 Q. Yes.

4 A. So "within" to me means it's not after or
5 it's talking about within 4 to 7 days. So it would
6 be within -- it's almost the same thing as within
7 seven days. So to me, that means first, second,
8 third, fourth, fifth, sixth, and seventh day.

9 Q. Okay. Could you give us a brief summary of
10 what is meant by a stroke?

11 MR. WILKERSON: Objection to form.

12 A. A stroke means that there is damage to the
13 cells in the brain, and it can be due to disruption
14 in blood flow to the brain or it can be due to
15 bleeding into the brain. So the first form of
16 stroke is called ischemic stroke, and the second
17 form of stroke is called hemorrhagic stroke.

18 Ischemic stroke can be due to blockage in
19 the vessels, or it can be due to embolism into the
20 brain. And the most common form of embolism is
21 because of atrial fibrillation that happens in some
22 patients who have heart disease, and that causes

1 clot formation in the heart that can dislodge and go 09:54:12
2 to the brain. 09:54:15

3 Q. And could you give us a similar summary for 09:54:18
4 myocardial infarction? 09:54:21

5 A. So myocardial infarction means that there is 09:54:21
6 damage to the cells of the heart. And the most 09:54:24
7 common cause of myocardial infarction, at least in 09:54:27
8 this country, now probably in the world, is 09:54:31
9 atherosclerotic heart disease, and that's due to 09:54:36
10 blockage in the coronary vessels. And the most 09:54:39
11 common cause of myocardial infarction is disruption 09:54:43
12 of blood flow due to damage to the lining of the 09:54:46
13 atherosclerotic plaque and formation of thrombus at 09:54:52
14 the site. 09:54:56

15 Q. And you've already educated us a bit on 09:54:57
16 pericarditis, but if you could give us another brief 09:55:00
17 summary. 09:55:03

18 A. Sure. So pericarditis refers to the 09:55:03
19 inflammation of the lining of the heart. For some 09:55:06
20 reason, mammals or mammals have this sack around 09:55:12
21 their heart. We don't really understand the 09:55:15
22 function of this sack. But this sack can get 09:55:18

1 inflamed, and that can cause pericarditis. And if
2 it is an acute process, it usually goes away, but it
3 can turn into chronic pericarditis. And sometimes
4 it can lead to fluid accumulation within the sack,
5 and that's called paracardial effusion.

6 Q. And is it fair to say that the three
7 conditions you just described all relate to an
8 inflammatory condition?

9 A. You mean stroke, myocardial infarction, and
10 pericarditis. So these are complex processes. They
11 are not just due to inflammation. There are a
12 number of processes that contribute to all of them.
13 But inflammation plays a role in all of them, yes.

14 Now, let me step back. Hemorrhagic stroke
15 is generally not because of an inflammatory process.
16 It can turn into an inflammatory process to remodel
17 the brain after bleeding. But most of the ischemic
18 events related to the brain can be due to an
19 inflammatory process.

20 Q. And is stroke and myocardial infarction more
21 closely related together than pericarditis?

22 A. In the terms of their pathogenesis, yes.

1 Q. And what are the differences between how you 09:56:49
2 would treat for pericarditis relative to stroke 09:56:54
3 or -- stroke and myocardial infarction? 09:57:00

4 A. Right. As I mentioned, myocardial 09:57:04
5 infarction and stroke are complex processes. They 09:57:06
6 are due to multiple pathological processes that end 09:57:09
7 up leading to disruption of blood flow to the brain 09:57:12
8 or the heart, so you try to target all of those 09:57:16
9 processes and to reduce risk factors. So those 09:57:20
10 include high blood pressure, diabetes, high 09:57:24
11 cholesterol, to large extent, inflammation. And, 09:57:28
12 you know, of course, you try to reduce other risk 09:57:35
13 factors. If the patient is a smoker, you ask them 09:57:38
14 to stop smoking. You ask them to lose weight and 09:57:40
15 exercise. So you try to take, you know, 09:57:44
16 multi-pronged approach to these processes, and try 09:57:48
17 to reduce all of the risk factors. 09:57:51

18 In terms of pericarditis, it's mostly an 09:57:54
19 inflammatory process. And what you are trying to do 09:57:56
20 is to reduce the inflammation. And you give them 09:57:59
21 anti-inflammatory medications. 09:58:02

22 Q. Do you personally treat any patients with 09:58:10

1	any of those three conditions?	09:58:12
2	A. Yes.	09:58:13
3	Q. Which ones?	09:58:14
4	A. Well, of course, myocardial infarction. We	09:58:16
5	treat them on a regular basis. We see a lot of	09:58:19
6	patients with pericarditis. In fact, after COVID,	09:58:22
7	this has turned into a major problem in a lot of	09:58:26
8	patients. We get patients post COVID and some of	09:58:31
9	them, we have to look very carefully to see if they	09:58:34
10	have pericarditis. They undergo MRI and extensive	09:58:38
11	studies.	09:58:42
12	In terms of stroke, I'm not a neurologist,	09:58:42
13	but we do have patients who have had a history of	09:58:45
14	stroke, and we make sure that their medications are	09:58:48
15	maximized.	09:58:51
16	Q. And you may have already answered this, but	09:58:54
17	is there a difference between how pericarditis would	09:58:58
18	be treated and how stroke -- excuse me. We did ask	09:59:00
19	that.	09:59:03
20	So what is the usual journey of patients	09:59:05
21	that have myocardial infarction?	09:59:08
22	A. So you are saying after they present with	09:59:12

1 myocardial infarction?

09:59:15

2 Q. Correct.

09:59:16

3 A. So it really depends on the presentation.

09:59:16

4 If they have ST elevation MI, that means they have

09:59:19

5 significant damage that causes the segment of EKG --

09:59:24

6 which is called ST -- to be elevated. They are

09:59:29

7 taken directly to the cath lab. So even if it is in

09:59:32

8 the middle of the night, the cath lab gets

09:59:36

9 activated, they go to cath lab, and they get

09:59:39

10 angioplasty and stent placement.

09:59:42

11 If they have evidence of myocardial

09:59:45

12 infarction but there is no ST elevation, we usually

09:59:48

13 stabilize them medically, so they are given several

09:59:50

14 different medications, including antiplatelet

09:59:53

15 agents, which includes aspirin, sometimes Plavix.

09:59:57

16 They are also given anticoagulants, like heparin.

10:00:01

17 They are given beta blockers, sometimes ACE

10:00:06

18 inhibitors. We generally start them on statins.

10:00:09

19 And when the cath lab is available, we send them to

10:00:11

20 the cath lab to get the intervention to open up the

10:00:14

21 vessel.

10:00:18

22 Now, some of these patients may need more

10:00:19

1 extensive intervention, and they may go to surgery
2 to get cardiac bypass.

3 Q. And after the stents are placed in the cath
4 lab, what medications do you prescribe?

5 MR. WILKERSON: Objection. Form.

6 A. So antiplatelet therapy is what we use. So
7 aspirin plus Plavix or Brilinta is -- we call it
8 dual antiplatelet therapy. And they are also given
9 beta blockers. They're given ACE inhibitors, and
10 they're given statins. Those are -- statins are
11 like Lipitor, Crestor, those medications have been
12 shown to help them extensively.

13 Now, if they have other risk factors, like,
14 you know, high blood pressure, we try to get their
15 blood pressure under control. If they have
16 diabetes, of course, you know, SGL2 inhibitors. I
17 am sure you have seen, you know, those commercials
18 on TV. They work really well in some of these
19 patients, especially if they have heart failure. So
20 as cardiologists, now, we are giving a lot of
21 diabetes medications to our patients.

22 Q. And of the medications you mentioned, those

1	are prescribed in the hospital?	10:01:38
2	A. Most of them are.	10:01:41
3	Q. So the patient starts the medication while	10:01:42
4	they're at the hospital?	10:01:45
5	A. Again, the majority of them are, yes.	10:01:47
6	Q. And is that true for the statins?	10:01:50
7	A. The statins, yes, we start them in the	10:01:52
8	hospital.	10:01:55
9	Q. What's the typical time period for a	10:01:55
10	hospital stay after a myocardial infarction?	10:02:01
11	A. Right. So it really depends on the patient.	10:02:05
12	But most patients, the majority of them are	10:02:08
13	stabilized within two to three days, and they are	10:02:12
14	discharged within two to three days. That's the	10:02:16
15	common practice in this country. You know, I've	10:02:19
16	visited other countries, and I know they keep their	10:02:21
17	patients a lot longer. You know, I was in Poland a	10:02:24
18	few years ago, and they keep their patients for a	10:02:27
19	long time in the hospital, which is actually -- we	10:02:29
20	believe it's not a good practice. But in this	10:02:32
21	country, two to three days is the common practice.	10:02:34
22	Q. And why is that a bad practice, in your	10:02:36

1	view?	10:02:39
2	A. Well, keeping patients in the hospital is	10:02:40
3	not a good practice because they can get other	10:02:42
4	diseases, and it's -- not necessarily correlates	10:02:45
5	with better outcome. So ...	10:02:49
6	Q. And after a patient is discharged, what is	10:02:53
7	the usual journey for patients in the United States?	10:02:56
8	A. They follow up with their cardiologist. And	10:03:00
9	they are encouraged not to smoke, and we do	10:03:04
10	everything we can to prevent smoking and to ask them	10:03:10
11	to exercise and to lose weight. They are referred	10:03:14
12	to cardiac rehab if their insurance allows that, and	10:03:19
13	they follow with their cardiologist.	10:03:23
14	Q. And any medications that you started in the	10:03:25
15	hospital, do you typically then continue those on	10:03:28
16	after discharge?	10:03:31
17	A. Yes. So with dual antiplatelet therapy, we	10:03:32
18	generally stop Plavix or Brilinta within 12 months.	10:03:36
19	So after 12 months, we stop one of those	10:03:43
20	medications. I'm sorry. After 12 months, not	10:03:46
21	within 12 months.	10:03:49
22	Q. And is there, in the United States, an early	10:03:49

1 post-discharge period with closer follow-up than a

10:03:55

2 later discharge period with less supervision?

10:04:00

3 MR. WILKERSON: Objection. Form.

10:04:04

4 A. I'm sorry. I'm not following.

10:04:05

5 Q. Is there any transition so that after a

10:04:07

6 patient is discharged, the physician might monitor

10:04:10

7 the patient after they're discharged initially but

10:04:15

8 not so much later on?

10:04:20

9 A. Right. So if they become stabilized, I

10:04:21

10 generally see my patients within three to six

10:04:26

11 months. And then if they are stable, they are doing

10:04:29

12 well, I sometimes tell them you don't have to come

10:04:31

13 back for another year.

10:04:33

14 Q. So if you were to break that down, what's

10:04:36

15 the -- what's -- how would you define on the

10:04:39

16 spectrum of what's an initial period and a later

10:04:44

17 period? What would that breakdown be?

10:04:49

18 MR. WILKERSON: Objection. Form.

10:04:53

19 A. Well, it depends on if I have any openings

10:04:54

20 in my clinic, which is not very -- you know, not

10:04:57

21 very common these days, so they usually see a nurse

10:04:58

22 practitioner within the first three to six months.

10:05:01

1 And then they come to my clinic, and then I evaluate 10:05:04
2 them hopefully within six months. And then if 10:05:08
3 not -- and then I see them, if they are stable 10:05:12
4 sometimes I tell them, you know, come back and see 10:05:16
5 me in 12 months. 10:05:18

6 Q. Okay. 10:05:19

7 MR. LAURENCE: We've been going for a little 10:05:27
8 while. Do you want to take a break or are you good? 10:05:29

9 MR. WILKERSON: We can take a break. 10:05:32

10 THE WITNESS: Yeah. Thank you. 10:05:33

11 THE VIDEOGRAPHER: Going off the record at 10:05:36
12 10:04 a.m. 10:05:39

13 (A short break was had.) 10:05:40

14 THE VIDEOGRAPHER: Going back on the record 10:15:14
15 at 10:14 a.m. 10:15:16

16 BY MR. LAURENCE: 10:15:17

17 Q. Dr. Ardehali, I'm turning back to your 10:15:20
18 patent, the Ardehali patent, which is Exhibit 1058. 10:15:22

19 A. Okay. 10:15:26

20 Q. In your own words, please describe the 10:15:26
21 subject matter of the patent. 10:15:30

22 A. So this patent was on use of iron chelators, 10:15:39

1 so those are molecules that reduce iron levels, and 10:15:47
2 these were specifically targeting mitochondrial 10:15:50
3 iron. So they were cell permeable, and they could 10:15:55
4 get into the mitochondria. And the idea was that if 10:15:58
5 you reduce mitochondrial iron, you would reduce 10:16:02
6 the damage to the heart following myocardial 10:16:09
7 infarction. 10:16:11

8 Q. And could you turn to one of the last 10:16:11
9 pages -- it is the last page, page 39, in the right 10:16:14
10 column, column 34? 10:16:20

11 A. Yes. 10:16:22

12 Q. Toward the bottom of the page, there are 10:16:23
13 four claims. 10:16:25

14 Do you see those? 10:16:25

15 A. Yes. 10:16:26

16 Q. And can you tell me what Claim 1 recites? 10:16:27

17 A. So this basically talks about treating a 10:16:48
18 patient after myocardial infarction or during 10:16:51
19 cardiac ischemic with mitochondrial permeable iron 10:16:52
20 chelator. And in this specific case, we are 10:16:59
21 referring to 2, 2 prime-bipyridyl. So it's 10:17:02
22 b-i-p-y-r-i-d-y-l. And we refer to this as BPD. 10:17:10

1	Q. And in the first line of the claim, which is	10:17:15
2	on line 49, what is meant by "a method of treating a	10:17:19
3	subject"?	10:17:23
4	MR. WILKERSON: Objection to form.	10:17:24
5	A. It's describing a method of treating a	10:17:27
6	patient with this drug.	10:17:31
7	Q. And what is the therapeutic benefit?	10:17:33
8	A. Well, we are proposing that this would	10:17:37
9	reduce the damage to the heart.	10:17:41
10	Q. And does this patent describe the use of a	10:17:45
11	loading dose of the chelator?	10:17:48
12	MR. WILKERSON: Objection. Relevance.	10:18:01
13	A. Yeah, I have to read the patent. It's been	10:18:02
14	a while, but I can't remember if we included a	10:18:04
15	loading dose.	10:18:08
16	Q. Is it recited in any of the claims?	10:18:09
17	MR. WILKERSON: Same objection.	10:18:11
18	A. It doesn't talk about loading dose in one of	10:18:32
19	the claims.	10:18:35
20	Q. And would a loading dose be useful or	10:18:35
21	harmful to impacting mitochondrial iron in a	10:18:38
22	subject?	10:18:43

1	MR. WILKERSON: Objection. Relevance.	10:18:43
2	A. So you are talking about a loading dose of	10:18:45
3	an iron chelator for mitochondrial iron?	10:18:48
4	Q. Uh-huh.	10:18:54
5	A. I don't think we tested that in our studies.	10:18:54
6	Q. Does your patent teach excluding a loading	10:19:01
7	dose of the chelator?	10:19:05
8	MR. WILKERSON: Same objection.	10:19:06
9	A. I would have to read the whole patent, but I	10:19:07
10	don't think we included exclusion of a loading dose.	10:19:11
11	Q. If you could turn to page 4, do you see	10:19:19
12	figure 1 on page 4?	10:19:27
13	A. Yes.	10:19:29
14	Q. And if you could also turn to page 23,	10:19:30
15	line -- excuse me -- column 2?	10:19:50
16	A. Yes.	10:19:53
17	Q. Line 17 through 33, could you read that to	10:19:54
18	yourself?	10:19:57
19	A. Okay.	10:20:18
20	Q. How many days after ischemic reperfusion	10:20:18
21	procedure was the testing conducted?	10:20:24
22	MR. WILKERSON: Same objection.	10:20:26

1	A. Two days after surgery.	10:20:27
2	Q. And if you could turn to page 8, do you see	10:20:28
3	figure 5 on page 8?	10:20:38
4	A. Yeah, the pages are not numbered, but I see	10:20:42
5	figure 5.	10:20:45
6	Q. It's in the bottom right corner here.	10:20:46
7	A. Okay. I see it, yes.	10:20:48
8	Q. And if you could turn to page 24 and read to	10:20:50
9	yourself in column 3, lines 10 through 24, which	10:21:00
10	describes figure 5?	10:21:05
11	A. Okay.	10:21:33
12	Q. And what amount of time is described for the	10:21:34
13	assessment in figure 5?	10:21:36
14	MR. WILKERSON: Objection. Relevance.	10:21:37
15	A. So, again, this is 28 days after injury, but	10:21:42
16	I want to emphasize, we are looking at a completely	10:21:46
17	different process here compared to '063, just to	10:21:48
18	make relevance here clear. But yes, this is not	10:21:51
19	even related to what we did -- what was done in the	10:21:54
20	other patent.	10:21:57
21	Q. But why did you pick those two time periods?	10:22:07
22	MR. WILKERSON: Same objection.	10:22:01

1 A. Right. So that's what we generally do in
2 our basic research in the lab. What we do is we
3 look at acute injury, which is usually within two
4 days, and we also look at the effect after a chronic
5 process. So we sometimes look at the effect after
6 28 days to see if the mice are suffering from heart
7 failure. Or I'm sorry. Let me step back. From
8 cardiomyopathy.

9 Q. And was a clinical study conducted related
10 to the treatment in your patent?

11 A. So we are not doing -- a clinical study
12 hasn't been done, but, again, we are doing a study
13 with an iron chelator, not exactly the same iron
14 chelator, a different iron chelator. And what we
15 are doing or trying to do, if we get the funding, is
16 to look at the degree of atherosclerotic plaque in
17 patients after they are given iron chelators. And
18 the way we are doing it is that we are doing CT
19 angiogram to look at the degree of plaque formation
20 at six months and after 12 months after they are
21 given iron chelator.

22 Q. Okay. And on the first page of the Ardehali

1	patent, do you see your name listed as an inventor?	10:23:24
2	A. Yes.	10:23:26
3	Q. And do you see that there's another inventor	10:23:27
4	listed, is it Dr. Chang?	10:23:31
5	A. Yes.	10:23:33
6	Q. What was his contribution, do you recall?	10:23:34
7	A. So Jimmy Chang was an M.D., Ph.D. student in	10:23:35
8	my lab, and he contributed significantly to this	10:23:43
9	project. And I ask him to be listed as an inventor	10:23:46
10	on this patent. I didn't have to, but I thought it	10:23:51
11	was a good idea to include him. And, in fact, I	10:23:56
12	think all of my patents I have somebody else as a	10:23:59
13	co-inventor.	10:24:01
14	Q. Do you recall specifically what he	10:24:06
15	contributed?	10:24:08
16	A. Well, again --	10:24:10
17	MR. WILKERSON: Objection. Relevance.	10:24:11
18	You can answer.	10:24:12
19	THE WITNESS: Sorry.	10:24:13
20	A. I didn't do any of these experiments. I	10:24:15
21	don't do bench work anymore, but he's the one who	10:24:18
22	did all of these experiments.	10:24:21

1 Q. But did he contribute to something that's 10:24:23
2 specifically claimed in those four claims? 10:24:27

3 A. Right. Well, he did all the experiments. 10:24:29

4 Q. Okay. 10:24:31

5 A. So he is the one who did the actual 10:24:32
6 experiments. You know, people in my lab, they do 10:24:34
7 the experiments. They do the analysis. But I'm the 10:24:37
8 one who designed the experiments. I'm the one who 10:24:41
9 brings funding. And I'm the one who basically comes 10:24:43
10 up with the idea of these studies. That's why I'm 10:24:47
11 the principal investigator on grants and, on these 10:24:52
12 patents, I'm the inventor. 10:24:55

13 Q. Okay. So he did a lot of the work and so 10:24:56
14 you felt the need to include him as a co-inventor? 10:25:00

15 MR. WILKERSON: Objection. Form. 10:25:04

16 A. I didn't feel it was a need. You know, I 10:25:05
17 didn't have to. But I felt that Jimmy had done a 10:25:07
18 great job, and I generally do that with my -- with 10:25:11
19 the people in my lab, I include them as 10:25:14
20 co-inventors. 10:25:18

21 Q. Okay. 10:25:19

22 A. In fact, there was another patent that we 10:25:20

1 submitted recently and I -- it was, again, another 10:25:22
 2 M.D., Ph.D. student in my lab, and I contacted him 10:25:25
 3 and I said, "I want you to be a co-inventor on this 10:25:29
 4 patent." 10:25:32

5 Q. Did you publish an article related to the 10:25:35
 6 research in the Ardehali patent? 10:25:38

7 A. We have the couple of publications, yes. 10:25:41
 8 But the major one was published are in a journal 10:25:46
 9 called "EMBO Molecular Medicine." 10:25:50

10 Q. I'm handing you a copy of Exhibit 1059. 10:26:05

11 (Exhibit 1059 was marked for 10:26:05
 12 identification and was retained by counsel.) 10:26:14

13 A. Thank you. 10:26:14

14 Q. Which is this the article that you just 10:26:21
 15 referenced? 10:26:23

16 A. Yes. 10:26:24

17 Q. And is that the same Dr. Chang that's listed 10:26:24
 18 as the first author? 10:26:34

19 A. Yes. 10:26:35

20 Q. And are you listed as the corresponding 10:26:35
 21 author? 10:26:37

22 A. Yes. 10:26:38

1	Q. Is it accurate to say that, in some	10:26:44
2	circumstances, a co-author on one of your papers may	10:26:46
3	also be a co-inventor on a related patent?	10:26:50
4	MR. WILKERSON: Objection to form.	10:26:55
5	A. Did you ask is it common?	10:26:56
6	Q. For you.	10:26:58
7	A. Yes.	10:26:59
8	Q. So based on your experience as an inventor,	10:27:00
9	could you explain the difference being listed as an	10:27:11
10	author and being listed as co-inventors?	10:27:16
11	MR. WILKERSON: Objection. Form.	10:27:20
12	A. Well, many of these co-authors, they didn't	10:27:20
13	contribute significantly. They just -- or they did,	10:27:24
14	of course, all of them contributed significantly but	10:27:26
15	not to the degree that we felt they should be --	10:27:29
16	they should be co-inventors on this patent.	10:27:32
17	So, basically, what happened here is that	10:27:36
18	the idea was mine, I had funding for this -- for	10:27:38
19	this project. Jimmy did all of the experiments.	10:27:42
20	That was his Ph.D. thesis. He got a Ph.D. based on	10:27:47
21	the work he did in this project. And he stayed in	10:27:51
22	the lab after he got his Ph.D. and did postdoc in	10:27:56

1 the lab before he went back to medical school. So 10:27:59
2 he was the major driver of this project. And that's 10:28:03
3 why I felt that he should be a co-inventor on this 10:28:05
4 patent. 10:28:10

5 But I want to mention there are a lot of 10:28:16
6 labs that don't have that practice. Just the senior 10:28:19
7 author is the inventor of the patent. 10:28:21

8 Q. What do you mean by that? 10:28:26

9 A. Well, I've seen a lot of patents where just 10:28:27
10 a senior author is listed as the patent holder. 10:28:30

11 Q. I'm handing you a copy of Exhibit 1005, 10:28:53
12 which is the document that is referred to as the 10:28:57
13 Bouabdallaoui article. 10:29:05

14 Are you familiar with this paper? 10:29:07

15 A. Yes. 10:29:09

16 Q. And how many authors are listed here? 10:29:09

17 (Exhibit 1005 was marked for 10:29:09
18 identification and was retained by counsel.) 10:29:26

19 A. 24. 10:29:26

20 Q. Is this -- do you have any personal 10:29:26
21 knowledge about who did what among the authors 10:29:37
22 listed for the Bouabdallaoui article? 10:29:40

1	A. Well, based on how the authors are listed	10:29:45
2	and how the senior author is listed, I would say	10:29:49
3	Dr. Tardif was the principal investigator who	10:29:58
4	probably was responsible for the funding and for the	10:30:00
5	design of the project. Doctor B -- can I refer to	10:30:07
6	her as Dr. B?	10:30:14
7	Q. Yes.	10:30:16
8	A. Dr. B was responsible for most of the	10:30:16
9	analyses and maybe the writing of the paper, but the	10:30:19
10	lead author here is Dr. Tardif.	10:30:22
11	Q. And of the 24 authors, did any of them	10:30:26
12	inform you of the process that was used to list the	10:30:29
13	individuals as authors?	10:30:32
14	A. I haven't talked to any of them, no.	10:30:33
15	Q. So you're not acquainted with any of them?	10:30:37
16	A. No.	10:30:39
17	Q. Are you acquainted with Dr. Tardif?	10:30:39
18	A. I have not had any communication with him,	10:30:41
19	no.	10:30:44
20	Q. So other than your knowledge of industry	10:30:44
21	practice, is it fair to say that you don't have any	10:30:51
22	firsthand or personal knowledge regarding the	10:30:53

1 process of selecting the authors? 10:30:56

2 MR. WILKERSON: Objection. Form. 10:30:57

3 A. You mean for this paper? 10:30:58

4 Q. Yes. 10:31:00

5 A. Well, I have read Dr. Tardif and Dr. B's 10:31:01
6 declaration, and what they described is what is 10:31:06
7 common practice in our field. And, again, you know, 10:31:09
8 I have published a lot of papers. I have served on 10:31:16
9 the editorial boards of journals. And I'm the 10:31:19
10 deputy editor of one of probably the most respected 10:31:23
11 journal for physician scientists. 10:31:26

12 So I'm familiar how the system works and 10:31:29
13 what it means if somebody is the corresponding 10:31:32
14 author, which means the lead author. That person is 10:31:34
15 the one we would contact, you know, as a journal if 10:31:38
16 there is an issue. And we know that person is 10:31:43
17 responsible for the content of the paper. 10:31:46

18 There are cases where there are issues with 10:31:49
19 some of the figures that -- for the papers that come 10:31:55
20 to our journals, and we always contact the lead 10:31:58
21 author, who is the corresponding author, because 10:32:01
22 that person is eventually responsible for all the 10:32:05

1 content in the paper.

10:32:07

2 And in this paper, I would say, based on
3 what I'm seeing here and based on the declaration
4 from Dr. Tardif and Dr. B, I know that the lead
5 author is Dr. Tardif.

10:32:09

10:32:13

10:32:19

10:32:24

6 Q. And I noticed that, in your article that's
7 Exhibit 1059, you list yourself last.

10:32:27

10:32:32

8 Is that your common practice?

10:32:36

9 A. Yes.

10:32:37

10 Q. And is that common practice for the
11 corresponding author to list themselves last?

10:32:37

10:32:44

12 A. Not always. Sometimes they do. Sometimes
13 they don't.

10:32:47

10:32:50

14 Q. What drives that difference?

10:32:51

15 A. I don't think there is a defined factor that
16 drives it. Some people like to be included as the
17 last author. In my lab, every paper that comes out
18 of my lab, I'm the last author.

10:32:56

10:33:01

10:33:04

10:33:08

19 Q. So is it safe to say that your opinions
20 regarding inventorship of the '063 patent are based
21 on the declarations from Dr. Tardif,
22 Dr. Bouabdallaoui, and your industry experience?

10:33:23

10:33:26

10:33:30

10:33:34

1	MR. WILKERSON: Objection to form.	10:33:37
2	A. I would say -- I wouldn't say industry	10:33:38
3	experience. I would say my academic experience and	10:33:41
4	my experience as being on editorial board of a	10:33:44
5	number of journals and being the deputy editor of a	10:33:51
6	major journal in our field.	10:33:55
7	Q. But is it fair to say that it's not based on	10:33:57
8	any firsthand knowledge of what occurred in	10:34:01
9	Dr. Tardif's lab?	10:34:05
10	MR. WILKERSON: Objection. Asked.	10:34:07
11	A. Well, first of all, I don't think Dr. Tardif	10:34:09
12	has a lab or a wet lab. He probably has a group.	10:34:12
13	And secondly, in their declaration, they	10:34:16
14	went through the process very clearly. And they	10:34:18
15	explained what the process involved, and Dr. Tardif	10:34:21
16	explained it very, you know, in detail, how he	10:34:24
17	designed and how he brought the group together for	10:34:28
18	this project.	10:34:32
19	Q. But based on your experience in your team,	10:34:37
20	where you have an overlap of individuals who could	10:34:44
21	be co-authors, they could be co-inventors, is it	10:34:49
22	possible that someone else came up with the	10:34:53

1	referenced time periods other than Dr. Tardif?	10:34:56
2	MR. WILKERSON: Objection to form.	10:35:00
3	A. Somebody came -- sorry. Could you repeat	10:35:06
4	that?	10:35:09
5	Q. Based on your experience, in your team where	10:35:09
6	you indicated that you have an overlap of	10:35:19
7	individuals who could be co-authors and	10:35:21
8	co-inventors, is it possible that someone else came	10:35:26
9	up with the reference time periods that are recited	10:35:29
10	in the claims of the '063 patent other than	10:35:32
11	Dr. Tardif?	10:35:35
12	MR. WILKERSON: Objection to form.	10:35:36
13	A. I would say it's very unlikely. Extremely	10:35:37
14	unlikely. This is -- you know, this is common	10:35:41
15	practice in our field, and we -- the senior author	10:35:44
16	is almost always the lead author. I don't	10:35:47
17	understand why anybody else would be the senior	10:35:50
18	author if they are not the lead author.	10:35:53
19	And to be honest, I don't even know the	10:36:02
20	distinction, to be honest. So ...	10:36:05
21	Q. Distinction between what?	10:36:07
22	A. Senior author and the lead author or	10:36:09

1 corresponding author. To us, those are the same
2 thing.

3 Q. And in terms of inventorship, what is the
4 understanding of the difference between being
5 co-inventors and co-authors?

6 MR. WILKERSON: Objection. Form.

7 A. So co-inventors means that their names
8 appear on the patent. Co-authors means that their
9 names appear on a paper.

10 Q. But what's the basis for deciding who is
11 listed --

12 MR. WILKERSON: Objection. Legal
13 conclusion.

14 Sorry.

15 Q. -- as co-inventor and co-authors?

16 MR. WILKERSON: Objection. Legal
17 conclusion.

18 A. At least in my case, it depends on what the
19 senior author or principal investigator decides.

20 Q. Okay.

21 A. And I would say that's probably common
22 practice.

1 So just to maybe give you some background,
2 if someone from my lab contacts, you know, the
3 patent office at Northwestern and says they want to
4 have a patent -- this has never happened, but I
5 would be really surprised if the patent office at
6 Northwestern would pursue that. They want to hear
7 from the principal investigator. And this is common
8 at every institution. The lead author, the lead
9 investigator is the one who starts the patent
10 process.

11 Q. And they control who's listed?

12 MR. WILKERSON: Objection. Legal
13 conclusion.

14 A. Again, in my experience in what I have done,
15 yes.

16 Q. In what journal was the Bouabdallaoui paper
17 published in?

18 A. European Heart Journal.

19 Q. Have you ever published anything in the
20 European Heart Journal?

21 A. I think I have. I can't remember.

22 Q. Do you publish in many, many different

1 journals, or do you have certain ones that you like 10:38:07
2 over others? 10:38:11

3 A. Well, in our field, of course, we always 10:38:12
4 shoot for cell, science, nature journals and their 10:38:15
5 sub- -- you know, their daughter journals. So 10:38:19
6 that's what my lab people usually target. If we 10:38:20
7 have something that is more clinically relevant, we 10:38:25
8 target either circulation or European Heart Journal. 10:38:29

9 In fact, let me step back. I'm pretty sure 10:38:32
10 we have a publication in European Heart Journal, at 10:38:35
11 least one. And so yes, it depends on what the 10:38:38
12 subject field is. 10:38:40

13 Q. And the cell science nature journals, those 10:38:41
14 are the premier journals in your field? 10:38:50

15 MR. WILKERSON: Objection. Form. 10:38:54

16 A. Yes. 10:38:55

17 Q. Is there generally an understood pecking 10:38:55
18 order for publications in your field? 10:38:58

19 A. Really depends on the lab, yes. But if you 10:39:02
20 are talking about the impact factor and prestige, 10:39:05
21 yes, those are the top journals in our field. 10:39:08

22 Q. What are some of the others? 10:39:10

1 A. Well, again, JCI, the journal we have is one
2 of the top journals. I mentioned the daughter
3 journals for these three: Cell, science, nature.
4 And if you go into the clinical area, New England
5 Journal of Medicine, Lancet. Those are -- JAMA.
6 Those are top journals. And in our field, in basic
7 science, we also have PNAS. And yeah, those are the
8 major journals in our field.

9 Q. And where would the European Heart
10 Journal -- where would you categorize them in that
11 pantheon?

12 A. Well, European Heart Journal has a very high
13 impact factor, but it's mostly because of their
14 clinical papers that they publish and also because
15 of guidelines that they publish. It's a very highly
16 respected journal, and they publish a lot of
17 clinical papers in the field of cardiology.

18 Q. What is meant by post hoc analysis?

19 A. That means going into the data obtained from
20 a Phase 3 clinical study most of the time and doing
21 analysis of the data to answer a specific question.

22 Q. And is that the same as a secondary

1	analysis?	10:40:44
2	A. In general, yes. Yeah. Generally yes.	10:40:46
3	Q. And is that the same as a subanalysis?	10:40:50
4	A. Yeah. I have not heard that term a lot, but	10:40:55
5	yes, that sounds about -- to be the same as the	10:40:59
6	other two terms.	10:41:01
7	Q. Have you worked on any -- do you mind if I	10:41:02
8	use the acronym PHA for post hoc analysis?	10:41:05
9	A. Sure. I have not done anything on post hoc	10:41:10
10	analysis, no.	10:41:14
11	Q. How about in your lab?	10:41:15
12	A. No, but we have looked at databases of	10:41:19
13	tissue samples. They were not -- that wasn't	10:41:25
14	studying a clinical trial, but we have looked at	10:41:32
15	tissue samples and have analyzed them for	10:41:34
16	different -- to answer different questions.	10:41:37
17	Q. And that was in the field of cardiology?	10:41:38
18	A. Yes.	10:41:40
19	Q. But it wasn't published, or did you say it	10:41:41
20	was?	10:41:44
21	A. No. They have been published.	10:41:44
22	Q. Oh, okay.	10:41:45

1	In the Bouabdallaoui paper, there are	10:41:55
2	time-to-treatment initiation time points that are	10:41:56
3	described.	10:42:01
4	Are you familiar with those?	10:42:01
5	A. Yes.	10:42:02
6	Q. And were those same time-to-treat initiation	10:42:03
7	time points described in COLCOT?	10:42:07
8	MR. WILKERSON: Objection. Foundation.	10:42:14
9	A. You mean in the study?	10:42:16
10	Q. Yes.	10:42:17
11	A. In the publication?	10:42:18
12	Q. Yes.	10:42:20
13	A. In the publication, they didn't look at	10:42:21
14	these time points specifically. But this was a	10:42:23
15	post hoc analysis of COLCOT.	10:42:27
16	Q. What are typical limitations of post hoc	10:42:32
17	studies?	10:42:36
18	A. Well, they're not randomized clinical	10:42:40
19	trials. You know, they cannot -- they don't have	10:42:43
20	the confidence -- or the data do not provide the	10:42:46
21	confidence that Phase 3 clinical trials do. But in	10:42:50
22	many cases, we use post hoc analysis to -- for our	10:42:54

1 clinical practice. So we have used that in the
2 past.

3 Q. And do any of those limitations apply to the
4 Bouabdallaoui paper?

5 A. Well, as I said, yes, this is not a
6 randomized clinical trial. It's a post hoc
7 analysis. So you know, it's not -- the results are
8 not as -- you know, as -- they are not like the
9 results of a Phase 3 clinical trial.

10 Q. So what can be done to overcome limitations
11 of post hoc analyses?

12 A. Well, short of doing a randomized clinical
13 trial, I don't see there is any other way.

14 Q. So if you were reading a research paper
15 based on a statistical analysis of a
16 non-pre-specified subgroup, such as a post hoc
17 subgroup analysis, what specific information would
18 you look for to validate the results?

19 MR. WILKERSON: Objection. Form.

20 A. I don't think there is a specific factor,
21 but I look at the quality of the paper. And as I
22 said earlier, post hoc analyses have changed our

1 practice. Not just mine, a lot of -- even the 10:44:19
2 practice that is recommended in guidelines, some of 10:44:23
3 them are based on post hoc analysis. So they -- in 10:44:26
4 some cases, they provide valuable information but 10:44:30
5 not in every case. 10:44:34

6 Q. So in the Bouabdallaoui paper on page 1, the 10:44:51
7 abstract that's listed there, it lists the TTI in 10:44:59
8 the fifth line down of the abstract. 10:45:07

9 Do you see that? 10:45:10

10 Where the abstract -- by that, I'm referring 10:45:11
11 to the section that says "Methods and Results." 10:45:13

12 And then on the fifth line -- 10:45:16

13 A. Yes. 10:45:18

14 Q. -- it says TTI. It's got -- is that greater 10:45:18
15 than 3? 10:45:22

16 A. Less than 3. 10:45:23

17 Q. Less than 3. 10:45:24

18 And then 4 to 7. And then greater than 10:45:25
19 8 days; is that correct? 10:45:29

20 A. Yes. 10:45:30

21 Q. And as listed there, does the 4 to 7 days 10:45:30
22 mean the same as within 4 to 7 days? 10:45:39

1	A. Not in this case, no.	10:45:43
2	Q. Why is that?	10:45:45
3	A. Because it's specifically referring to 4 to	10:45:47
4	7 days.	10:45:51
5	Q. Okay. Let's look at table 2, which is on	10:45:51
6	page 5 or 4096.	10:46:11
7	Do you see that?	10:46:18
8	A. Yes.	10:46:18
9	Q. Can you describe what table 2 tells you?	10:46:19
10	A. So these are baseline characteristics of	10:46:24
11	patients in the -- according to the	10:46:27
12	time-to-treatment initiation, so for 0 to 3 days, 4	10:46:31
13	to 7 days, and more than 8 days. And then it has	10:46:35
14	the P value for each one of them.	10:46:39
15	Q. Okay. And what are the different factors	10:46:42
16	that are listed?	10:46:50
17	A. So characteristics are age, male sex, BMI,	10:46:52
18	current smoking, history of hypertension, history of	10:46:59
19	diabetes, prior MI, prior PCI, prior CABG, prior	10:47:02
20	heart failure, prior stroke or TIA, PCI associated	10:47:09
21	with the index event, medication use. And	10:47:15
22	underneath that, there is aspirin. Under	10:47:19

1	antiplatelet agent, statin beta blocker. Time from	10:47:21
2	index MI to randomization, days. Time from index MI	10:47:25
3	to PCI, days. And time from PCI to randomization in	10:47:32
4	days.	10:47:37
5	Q. Okay. And why is there an increase listed	10:47:37
6	for the age as you go across the three time periods?	10:47:44
7	MR. WILKERSON: Objection to form.	10:47:49
8	A. Why is there an increase?	10:47:53
9	Q. Yeah.	10:47:55
10	A. Well, those are the characteristics of those	10:47:56
11	patients.	10:47:59
12	Q. Okay. And the same question for those that	10:48:02
13	are current smokers.	10:48:05
14	MR. WILKERSON: Objection. Form.	10:48:08
15	A. Again, that's the characteristic of those	10:48:15
16	patients.	10:48:17
17	Q. Do you see any difference between the three	10:48:20
18	categories for current smokers?	10:48:24
19	A. Right, so it looks like patients who were	10:48:27
20	started on colchicine after 8 days, they had a	10:48:35
21	significantly lower number of smokers. Or I'm	10:48:41
22	sorry, lower percentage of smokers.	10:48:49

1 Q. Okay. And then let's look at the same for
2 hypertension. Can you give us a narration on that
3 one?

4 A. Sure. So it looks like patients who had --
5 patients who had history of hypertension, they were
6 more -- okay. Let me step back.

7 So patients who were started on colchicine
8 after 8 days, they had a higher incidence or high
9 percentage of hypertension compared to those within
10 the 4 to 7 days and those within the first 3 days.

11 Q. Okay. Can you provide a similar analysis
12 for diabetes?

13 A. Same thing. That those who were at 8 days,
14 they appear to have more percentage of diabetes
15 compared to those who were in the 4 to 7 days versus
16 those who were in 3 -- 0 to 3 days.

17 Q. And then for prior myocardial infarction?

18 A. Same thing. It looks like those who were --
19 started after 8 days, they had a higher prior MI
20 compared to those within 4 to 7 days versus those 0
21 to 3 days.

22 Q. And prior PCI?

1	A. So same thing. It looks like those who were	10:51:01
2	started after 8 days, they had a higher incidence of	10:51:03
3	prior PCI compared to those who were started 4 to	10:51:07
4	7 days versus those who were started 0 to 3 days.	10:51:13
5	Q. And for prior CABG?	10:51:17
6	A. It doesn't look like there was a difference.	10:51:18
7	Q. Okay. Prior heart failure?	10:51:20
8	A. Same thing, that those who were after	10:51:26
9	8 days, they had a higher incidence.	10:51:29
10	Q. And then for prior stroke?	10:51:32
11	A. There was no difference.	10:51:34
12	Q. So as you've reviewed the data in table 2,	10:51:58
13	does this show that the 0 to 3 group had more	10:52:03
14	favorable characteristics?	10:52:06
15	MR. WILKERSON: Objection. Form.	10:52:08
16	A. Sorry. Give me one second. I need to look	10:52:24
17	at something.	10:52:26
18	So this was actually discussed in the paper.	10:52:58
19	So if you look at page 4. So in the column on the	10:53:04
20	left-hand side, the paragraph that starts with	10:53:16
21	"Baseline characteristics," it says, [As read]	10:53:20
22	Baseline characteristics, according to TTI strata,	10:53:23

1 are shown in this table 2. Patients in whom therapy 10:53:27
2 was initiated between days 0 to 3, when compared 10:53:30
3 with those at days 8 to 30, were younger and more 10:53:34
4 often active smokers, had less commonly hypertension 10:53:39
5 and diabetes but underwent more often PCI associated 10:53:46
6 with the index MI. 10:53:49

7 So there were some features that were 10:53:52
8 more -- you know, more favorable in 0 to 3, but 10:53:54
9 there were also some, you know, serious features or 10:53:57
10 characteristics with respect to their heart disease 10:54:01
11 that was more, you know, severe in those who were in 10:54:04
12 the group day 0 to 3. 10:54:09

13 Q. What do the P values in table 2 mean? 10:54:19

14 MR. WILKERSON: Objection. Foundation. 10:54:26

15 A. So there are two P values. One of them it 10:54:28
16 says PA, the other one says PB. So PA's group 10:54:32
17 comparison TTI 0 to 3 versus TTI 4 to 7 versus TTI 10:54:36
18 greater than 8 days. So I think PA refers to P 10:54:43
19 value when comparing all three of them. So that was 10:54:52
20 probably ANOVA test they did. 10:54:51

21 And then PB refers to the group comparison 10:54:57
22 TTI 0 to 3 versus TTI more than 8 days. 10:55:00

1	THE WITNESS: ANOVA is A-N-O-V-A.	10:55:04
2	Q. So why these two P values? Why no P values	10:55:13
3	for individual interactions of the 4-to-7-day group	10:55:18
4	with the other two groups?	10:55:22
5	MR. WILKERSON: Objection. Form.	10:55:26
6	A. Well, this is what the authors wanted their	10:55:35
7	message to be. First they wanted to compare all	10:55:38
8	three columns or three groups, and then, in addition	10:55:41
9	to that, they wanted to specifically compare TTI 0	10:55:46
10	to 3 versus TTI greater than 8 days. So they may	10:55:50
11	have done other comparisons but they felt these two	10:55:55
12	were the most important for their message.	10:55:59
13	Q. So do you see that table 2 gives P values	10:56:14
14	for every line apart from time from index MI to	10:56:16
15	randomization?	10:56:21
16	A. Well, there is a dashed line for some of	10:56:30
17	these columns. And for time from index MI to	10:56:33
18	randomization, there is a dashed line under PA and	10:56:37
19	there's no number under PB.	10:56:42
20	Q. But why do you think no P values are given	10:56:43
21	there?	10:56:47
22	MR. WILKERSON: Objection to form.	10:56:47

1	A. You know, I have to read the paper carefully	10:56:52
2	to see why, if there was a reason behind it. But if	10:56:55
3	I had to guess, I would say they couldn't make the	10:57:06
4	comparison for those groups, for that specific	10:57:08
5	characteristic.	10:57:13
6	Q. Why do you think they couldn't make it?	10:57:15
7	MR. WILKERSON: Objection. Form.	10:57:18
8	A. Why they couldn't do the statistics?	10:57:19
9	Q. Yes.	10:57:23
10	A. Probably because the basic elements needed	10:57:23
11	to do a statistical analysis wasn't met.	10:57:27
12	Q. If you could turn the page to the next page,	10:57:38
13	which is 4097, or page 6 as numbered in the exhibit,	10:57:42
14	do you see table 3?	10:57:50
15	A. Yes.	10:57:53
16	Q. What are the P values for in table 3?	10:57:53
17	Excuse me.	10:58:01
18	What are the P values? Yeah, what are the P	10:58:01
19	values for? Sorry?	10:58:04
20	MR. WILKERSON: Objection to form.	10:58:06
21	A. So what they are doing here, they are	10:58:10
22	comparing each group that we discussed in table 2	10:58:12

1 versus placebo. And for each column, they are 10:58:16
2 reporting the P value for this comparison between 10:58:21
3 that group specifically versus placebo. 10:58:25

4 Q. And why does table 3 not have the same P 10:58:30
5 values as table 2? 10:58:36

6 A. So table 2 was not a comparison against 10:58:37
7 placebo. This was comparison between the groups 10:58:40
8 with respect to the time to initiation. 10:58:46

9 Q. And how would you interpret the results in 10:58:51
10 table 3 versus the results in table 2? 10:58:53

11 A. Right, so table 2 was reported to provide 10:58:56
12 the baseline characteristics of these patients. 10:59:01
13 Table 3 is the result of the efficacy studies. So 10:59:05
14 table 2 is not the report of the efficacy of 10:59:14
15 colchicine, while table 3 is providing the efficacy 10:59:17
16 of colchicine for each group when they were compared 10:59:20
17 to placebo. 10:59:23

18 Q. If you're missing the P values of table 2 10:59:26
19 and table 3, how does that change how you would 10:59:30
20 interpret the results? 10:59:32

21 MR. WILKERSON: Objection. Form. 10:59:33

22 A. Can you point to me where the P value is 10:59:34

1	missing in table 3?	10:59:40
2	Q. What I mean is the table 2 P values of PA	10:59:44
3	and PB are not in table 3; is that correct?	10:59:49
4	A. Sorry. I don't understand the question.	10:59:57
5	There shouldn't be PA, PB in table 3.	10:59:59
6	Q. Does it make sense to you that a trial, the	11:00:13
7	COLCOT trial that was testing low-dose colchicine	11:00:18
8	over the course of multiple years, that it would be	11:00:21
9	effective in the 0-to-3-day group but not effective	11:00:25
10	in the 4-to-7-day group or the greater-than-8-day	11:00:29
11	group?	11:00:32
12	MR. WILKERSON: Objection to form.	11:00:32
13	A. Does it make sense to me?	11:00:33
14	Q. Uh-huh. Correct.	11:00:36
15	A. Well, the data is very valuable, and if I	11:00:38
16	had to explain the, you know, molecular basis, I	11:00:45
17	would say yes, it makes sense.	11:00:49
18	Q. Can you elaborate?	11:00:51
19	A. So this is not -- this is not something I	11:00:54
20	knew before this study came out, so this study is a	11:01:00
21	step forward. But in addition to that, to answer	11:01:03
22	your question, yes, it makes sense that you start	11:01:07

1	this therapy early and you don't give a loading dose	11:01:09
2	and you start within 3 days after angioplasty in	11:01:15
3	patients who have myocardial infarction, it makes	11:01:21
4	sense that this is effective. But if you wait	11:01:25
5	longer, it also makes sense that, if you wait	11:01:27
6	longer, the effect may go away.	11:01:30
7	Q. But then it goes back up, doesn't it?	11:01:33
8	A. After 8 days?	11:01:35
9	Q. Yes.	11:01:36
10	A. So can you show me where it goes back up?	11:01:37
11	Q. Let's come back to it.	11:02:17
12	A. Okay.	11:02:23
13	Q. So let's look at figure 2 there on page 6.	11:02:24
14	Can you describe what that figure means?	11:02:39
15	A. So on the X-axis, they have time to	11:02:44
16	treatment in days and, on the Y-axis, they have	11:02:50
17	adjusted hazard ratio. And this is colchicine	11:02:53
18	versus placebo. And the line -- the solid line is	11:02:57
19	adjusted hazard ratio. Now, the dotted line is	11:03:06
20	something statisticians do. I can't explain it to	11:03:12
21	you in great detail, but to me that sounds like the	11:03:17
22	confidence interval range for this specific adjusted	11:03:22

1	hazard ratio at each time point.	11:03:26
2	Q. And what are hazard ratios?	11:03:33
3	A. Hazard ratio refers to the ratio of whether	11:03:35
4	or not an event is more likely in one group versus	11:03:39
5	the other. And if it is less than one, it usually	11:03:43
6	favours the treatment. If it is more than one, it	11:03:49
7	favours placebo.	11:03:52
8	Q. And what do you interpret from the solid	11:03:53
9	line?	11:03:55
10	A. So from solid line, it looks like --	11:03:56
11	Q. For each specific time period starting with	11:04:03
12	0 to 3 days.	11:04:10
13	A. Right. 0 to 3 days, it appears that the	11:04:11
14	hazard ratio is -- or the numbers favor treatment	11:04:15
15	with colchicine. And between 4 to 7 days, this line	11:04:19
16	continues to go up. And it gets to 7 days and it's	11:04:26
17	still up, up, and it continues to go up, up to 15 to	11:04:31
18	18 days, and then it goes back down to -- starts	11:04:36
19	to -- the curve starts going back down.	11:04:43
20	Q. So colchicine is an effective treatment in	11:04:45
21	the 0-to-3-day time period?	11:04:49
22	A. For what they were looking at, that's the	11:04:52

1	primary composite end point, yes.	11:04:54
2	Q. And what about the time period of 3 days to	11:04:56
3	looks like 8 days?	11:05:07
4	A. Right. So that didn't reach statistical	11:05:10
5	significance so that period was not shown to have	11:05:14
6	beneficial effects.	11:05:19
7	Q. So based on this chart, you wouldn't	11:05:20
8	prescribe colchicine for the time period 3 to	11:05:22
9	8 days?	11:05:26
10	MR. WILKERSON: Objection to form.	11:05:27
11	A. Well, here we have a range, right? I still	11:05:28
12	want to know what happens on day 4 and what happens	11:05:34
13	on day 5. And there's some data that help with	11:05:37
14	that. But I would -- based on this, what I would do	11:05:42
15	is I would try to start colchicine within the first	11:05:48
16	3 days.	11:05:51
17	Q. But you wouldn't do it at 4 days?	11:05:51
18	MR. WILKERSON: Objection. Asked.	11:05:53
19	A. Well, as I mentioned earlier, we don't have	11:05:55
20	the data for 4 days. We have the data for day 4 to	11:05:59
21	day 7. That's a range.	11:06:02
22	Q. But based on this information, you wouldn't	11:06:04

1 feel comfortable prescribing colchicine in the 4 to
2 7-day time period.

3 MR. WILKERSON: Objection. Asked.

4 A. Well, this data doesn't tell me specifically
5 about day 4. It tells me about day 4 to 7. And I
6 think there is some data that suggests day 4, the
7 benefit may still be there. So, again, what this
8 tells us as physicians we should try our best to
9 start treatment in the first 3 days.

10 Q. And what does the chart say?

11 When does it become plausible for you to
12 prescribe colchicine?

13 Based on this figure after several days
14 beyond the 0 to 3 window, what time period does this
15 chart indicate it's safe to prescribe colchicine at
16 a later date?

17 MR. WILKERSON: Objection. Form.

18 A. Well, first of all, this is not about safety
19 so I -- it doesn't tell me anything about when it is
20 safe.

21 Q. Well, doesn't it describe the hazard ratios?

22 A. Right. So that's for efficacy. We are

1 talking about -- this graph is about efficacy, not
2 about safety.

3 Q. So what point does it become an acceptable
4 range for efficacy?

5 MR. WILKERSON: Objection to form.

6 A. Right. So as I said earlier, they did --
7 this paper provides specific range for when to start
8 treatment. And what it tells us is that if you
9 start it in the first 3 days, it has beneficial
10 effects.

11 Q. And when do the beneficial effects kick in
12 again, according to this chart, after the 0 to
13 3 days?

14 A. There may be some efficacy at the end. Now,
15 I don't know how many patients there were in that
16 group. And so that number -- you know, so if you
17 look at day 29 to day 30, that P value may be less
18 than 0. And the, you know, dotted curve may go
19 below 1. But that's -- it's hard to tell only for
20 days 29 to 30. But it would be good to know how
21 many patients.

22 So this happens, you know, when the number

1 of patients gets small, so you may not get accurate
2 numbers. All this graph is telling us is that there
3 are three ranges. So if you are gonna make
4 conclusions about day 29 to day 30 based on this
5 graph, I totally disagree, because we don't have
6 enough information here. The only conclusion that
7 can be made from this graph is that this drug has
8 efficacy if it is given between day 0 and 3.

9 Q. But doesn't days 27 through 30 have,
10 essentially, the same adjusted HR as 0 to 3?

11 MR. WILKERSON: Objection. Asked.

12 A. Right. So if you look at day 27 to 30, I'm
13 not sure if the upper dotted line is below 1. It's
14 hard to tell. And I need to know how many patients
15 were in that group. So if you have very small
16 number of patients in that group, that can give you
17 misleading information. So I'm not gonna make a
18 conclusion based on this graph without that
19 information.

20 Q. But what basis leads you to feel comfortable
21 with the 0 to 3 when you don't feel comfortable with
22 the 27 to 30?

1 A. Sure. So I have the number. If you look at
2 table 3, it gives me the number. 1193 patients.
3 And there was statistics done specifically for that
4 group of patients. It gives me a P value and the
5 data is there. I don't have those numbers for days
6 27 to 30. I don't have a P value. I don't know how
7 many patients were included. And this study wasn't
8 even designed to look at days 27 to 30. So any
9 conclusion making -- saying that, you know, the
10 effect comes back on days 27 to 30 is incorrect.

11 Q. What else do you think is incorrect about
12 what's shown on figure 2?

13 MR. WILKERSON: Objection. Form.

14 A. Well, again, I'm not saying there is
15 anything incorrect shown in that figure. I'm saying
16 the conclusion you made is incorrect, that in
17 days 27 to 30, the efficacy comes back because that
18 comparison wasn't made. We have just limited
19 information in that bar graph, but it is incorrect
20 to make that conclusion that that difference is
21 significant.

22 But the graph is the graph. You know, the

1 graph is there. The information is correct. That
2 should be combined with the data that is provided in
3 table 3.

4 Q. And do you think that -- is there anything
5 you would take away from the peak that's shown
6 around day 15 or 16?

7 A. Right. So what I can tell you that this
8 graph was not designed to look at the peak, to look
9 at the curves, and make conclusions that you can --
10 you know, you can start medications at day 27 to 30
11 because it comes back down. You can't make that
12 conclusion because you don't know how many patients
13 you have in that group. There is no attempt in this
14 paper made to even look at that group.

15 All I can tell you, that this graph and
16 table 3, they were designed to look at just three
17 time points: Day 0 to 3, day 4 to 7, and greater
18 than 8 days. That's all the conclusions that can be
19 made here. If you try to make additional
20 conclusions, it's not based on science.

21 Q. So you don't -- so you disagree that
22 figure 2 shows greater efficacy in the 0 to 3 days

1 and then much lower efficacy several days later. 11:12:16

2 MR. WILKERSON: Objection. Form. 11:12:22

3 A. It is my conclusion -- and this is the 11:12:23

4 author's conclusion -- that there is efficacy if the 11:12:27

5 drug is started in the first 3 days, but the 11:12:30

6 efficacy goes away if you look at the group that 11:12:33

7 where -- where the drug was started 4 to 7 days or 11:12:39

8 after 8 days. 11:12:41

9 Q. And was COLCOT designed to study these time 11:12:44

10 periods? 11:12:51

11 A. The original study? 11:12:53

12 Q. Yes. 11:12:55

13 A. No. 11:12:55

14 Q. And how many patients are at the 0 to 3 or 11:12:55

15 actually in 0 to 2 days? 11:13:09

16 A. How many are in 0 to 2 days? Based on the 11:13:12

17 information I have here, I can't tell you. 11:13:15

18 Q. Okay. 11:13:17

19 A. That's the point I'm making here. You know, 11:13:18

20 we need more information if you want to make 11:13:21

21 conclusions regarding each time point, and that 11:13:25

22 would be our conclusion sitting here. That wouldn't 11:13:27

1 be the conclusion based on a statistician going over 11:13:29
2 the numbers and doing the kind of work that was done 11:13:36
3 in this paper. 11:13:39

4 Q. So does it make sense that a treatment, in 11:13:48
5 this case, low-dose colchicine that is meant as a 11:13:50
6 chronic therapy would work early on up to day 14 11:13:54
7 or 15, then it would be extremely deadly for a 11:13:58
8 couple of days, and then it would work again after 11:14:02
9 day 20 or so? 11:14:05

10 MR. WILKERSON: Objection. Form. 11:14:06

11 A. Sorry. I don't understand the question. 11:14:08
12 But I think, again, you are referring to this graph. 11:14:09
13 And I said it earlier that making these conclusions 11:14:12
14 that the effect, you know, goes away and then comes 11:14:18
15 back, that's not correct. You can't make that 11:14:21
16 conclusion. This graph doesn't give that message. 11:14:23
17 The paper made it very clear that there are three 11:14:25
18 time periods that should be included in the 11:14:29
19 conclusion of the data here, and that's day 0 to 3, 11:14:32
20 days 4 to 7, and greater than 8 days. That's all 11:14:38
21 the conclusion that can be made from this graph. We 11:14:41
22 don't have enough data to make additional 11:14:45

1 conclusions. And if you want to make additional 11:14:48
2 conclusions, you need to get additional data. And 11:14:50
3 that would be your conclusion, not the conclusion of 11:14:53
4 this paper. 11:14:55

5 Q. So you're comfortable concluding that 0 to 11:14:55
6 3 days has an efficacy established by the 11:15:00
7 Bouabdallaoui paper. 11:15:04

8 A. I would say that this paper shows that. And 11:15:05
9 the data is convincing to a lot of physicians to 11:15:10
10 practice that, and this may be sufficient for the 11:15:16
11 FDA to approve this drug for that time period. 11:15:19

12 Q. And you're not comfortable with the data 11:15:22
13 that's shown in figure 2 for any time period after 11:15:25
14 day 3? 11:15:29

15 MR. WILKERSON: Objection. Form. 11:15:30

16 A. No. I am. And I said it -- you know, I'm 11:15:31
17 comfortable with the conclusion the authors made. 11:15:35

18 Q. So you're comfortable with conclusion for 11:15:38
19 days 4 through 7? 11:15:42

20 MR. WILKERSON: Objection. Asked. 11:15:43

21 A. I'm comfortable with that time period 11:15:44
22 because the statistics were done, the number of 11:15:47

1 patients were included, the data is very clear, we 11:15:49
2 have all the data in table 2. And for that time 11:15:53
3 period, yes, I'm comfortable with the data. 11:15:57

4 Q. And then what time period are you not 11:15:59
5 comfortable with the greater than 8 days? 11:16:01

6 MR. WILKERSON: Objection to form. 11:16:04

7 A. I'm sorry. I didn't understand the 11:16:05
8 question. 11:16:07

9 Q. So table 3 shows three time periods. 11:16:07

10 A. Right. 11:16:12

11 Q. 0 to 3 days, 4 to 7 days, and then greater 11:16:12
12 than 8 days. And you said that you're comfortable 11:16:16
13 with the data shown in figure 2 that corresponds 11:16:19
14 with the 0 to 3-day time period, the 4 to 7-day time 11:16:21
15 period; is that correct? 11:16:27

16 A. Yes. 11:16:27

17 Q. And you're not comfortable with the data 11:16:28
18 that's shown for the greater than 8-day time period? 11:16:32

19 MR. WILKERSON: Objection to form. 11:16:34

20 A. No, I didn't say that. I'm comfortable with 11:16:35
21 that too. The number of patients are included. 11:16:38
22 They did good statistical analysis, and they made 11:16:41

1 the conclusion for those patients who were -- 11:16:45

2 medication was started after 8 days. 11:16:49

3 Q. Then why can't we make any conclusions based 11:16:53

4 on the adjusted HR line for the time period after 11:16:56

5 0 to 3 days or after the time period of 4 to 7 days? 11:16:59

6 MR. WILKERSON: Objection. Asked. 11:17:03

7 A. We can. And the conclusion was made. 11:17:04

8 Q. What are the conclusions that you make based 11:17:06

9 on that? 11:17:10

10 A. The conclusion -- the conclusion that I made 11:17:10

11 after reading this paper, the conclusion that the 24 11:17:12

12 authors on this paper made, the conclusion that the 11:17:15

13 scientific community, anyone who reads this paper 11:17:19

14 would make is that if you start colchicine after 11:17:22

15 8 days, you don't see the efficacy that you see if 11:17:25

16 you start the medication within 3 days. 11:17:29

17 Q. But that improves again at some time period. 11:17:34

18 A. Well, that's what I think is the incorrect 11:17:39

19 conclusion. Nowhere in this paper, they said, if 11:17:42

20 you start the medication between 27 to 30 days, you 11:17:45

21 get the efficacy. And there is a reason behind it. 11:17:49

22 They didn't include that because the data was not 11:17:52

1	analyzed.	11:17:55
2	Q. But COLCOT was meant as a long-term study;	11:17:56
3	correct?	11:18:00
4	A. That's correct.	11:18:00
5	Q. So as a doctor treating patients, how would	11:18:01
6	you treat your patients based on this data?	11:18:17
7	MR. WILKERSON: Objection. Form.	11:18:21
8	A. Right. So as I said earlier, any physician,	11:18:22
9	any scientist who reads this paper, the conclusion	11:18:25
10	would be that if you are looking for efficacy of	11:18:28
11	colchicine, in terms of reducing the primary	11:18:31
12	composite end point, which is cardiovascular events,	11:18:34
13	if you start it within the first 3 days, you would	11:18:39
14	have beneficial effects in your patients. That's	11:18:43
15	the conclusion. But if you started later, you would	11:18:45
16	not have -- you would not have that effect.	11:18:47
17	Q. But COLCOT established long-term benefits of	11:18:49
18	colchicine treatment; isn't that correct?	11:18:53
19	MR. WILKERSON: Objection to form.	11:18:56
20	A. Right. And this one does too if you're	11:18:57
21	talking about the course of treatment, yes. But	11:19:00
22	this study wasn't -- wasn't focused on the course of	11:19:02

1	treatment. This was focused on when to start the	11:19:07
2	treatment.	11:19:10
3	THE WITNESS: Can we take a break?	11:19:18
4	MR. LAURENCE: Yes.	11:19:20
5	THE WITNESS: Thank you.	11:19:21
6	THE VIDEOGRAPHER: Going off the record at	11:19:22
7	11:18 a.m.	11:19:24
8	(A short break was had.)	11:19:25
9	THE VIDEOGRAPHER: We're back on the record	11:33:33
10	at 11:32 a.m.	11:33:35
11	BY MR. LAURENCE:	11:33:37
12	Q. Handing you a copy of Exhibit 1020.	11:33:39
13	(Exhibit 1020 was marked for	11:33:39
14	identification and was retained by counsel.)	11:33:44
15	Q. Do you recognize this document?	11:33:44
16	A. Yes.	11:33:44
17	Q. And what is it?	11:33:59
18	A. This is the results of LoDoCo study.	11:34:01
19	THE WITNESS: L-o-D-o-C-o.	11:34:12
20	Q. And could you turn to page 13 of the PDF,	11:34:15
21	407 as numbered in the original publication.	11:34:18
22	Do you see table 1?	11:34:25

1	A. Yes.	11:34:26
2	Q. And in table 1, do you see the population	11:34:27
3	factors that are listed?	11:34:38
4	A. Yes.	11:34:39
5	Q. And do you see, seven down, PTCA?	11:34:40
6	A. Yes.	11:34:49
7	Q. What is PTCA?	11:34:54
8	A. It's percutaneous coronary angioplasty or	11:34:57
9	intervention.	11:35:04
10	Q. So do you mean it's the same as PCI?	11:35:04
11	A. Yes.	11:35:08
12	Q. How about CABG, is that different?	11:35:08
13	A. Yes. Let me step back. So sometimes people	11:35:12
14	refer to PTCA as angioplasty, and PCI can also	11:35:15
15	include stent. But, you know, the distinction is	11:35:21
16	not very clear. We usually refer to both as the	11:35:24
17	same thing.	11:35:26
18	Q. Okay.	11:35:26
19	A. And going back to your second question, yes,	11:35:27
20	CABG is different. CABG is bypass surgery so it	11:35:31
21	stand for coronary artery bypass surgery, and that's	11:35:35
22	when they open up the chest and they bypass the	11:35:38

1	vessels, and that's what cardiac surgeons do.	11:35:41
2	Q. Okay. And how many received PTCA?	11:35:46
3	A. You mean total? 115. No, I'm sorry. 138	11:35:53
4	plus 169.	11:36:00
5	Q. Okay. And in your own words, could you	11:36:15
6	describe the LoDoCo study?	11:36:19
7	A. Yes, so LoDoCo was a study where patients,	11:36:22
8	after -- or at least six months after they got --	11:36:36
9	they had myocardial infarction and they got	11:36:39
10	angioplasty or any coronary intervention, they were	11:36:44
11	randomized to get colchicine or no colchicine. This	11:36:49
12	was not a placebo-controlled study. And they looked	11:36:54
13	to see what their -- what the incidence of	11:36:58
14	cardiovascular events would be. So this was like	11:37:05
15	secondary events with colchicine.	11:37:08
16	Q. And what time period did it show efficacy	11:37:09
17	for?	11:37:13
18	A. So if you look at figure 2, that basically	11:37:17
19	shows you that the curves separate early on. So on	11:37:21
20	the X-axis is number of days. I don't know if the P	11:37:29
21	value or the confidence interval for 200 days was	11:37:38
22	significant between the two groups, but it looks	11:37:42

1 like, as early as 200 days or within the first year, 11:37:45

2 it appears that there is separation of the curves. 11:37:48

3 Q. Does it show efficacy after six months? 11:37:52

4 A. I have to read the paper carefully but, 11:38:02

5 based on that graph, I can't tell one way or the 11:38:04

6 other. Give me one second. Let me read these 11:38:09

7 paragraphs and I may be able to answer your 11:38:18

8 question. 11:38:20

9 Q. Okay. Could you read the conclusion on 11:38:20

10 page 10 that's listed in the abstract? 11:38:44

11 A. Sure. I wasn't finished here, but okay, 11:38:51

12 I'll come back. 11:38:53

13 Q. Oh, sorry. 11:38:55

14 A. So conclusion says, [As read] Colchicine 11:38:56

15 .5-milligram a day administered in addition to 11:38:58

16 statins and other standards secondary prevention 11:39:19

17 therapies appeared effective for the prevention of 11:39:02

18 cardiovascular events in patients with stable 11:39:07

19 coronary disease. 11:39:09

20 Q. So do you know what time period it showed 11:39:43

21 efficacy for? 11:39:53

22 A. Okay. So let me go back and finish what I 11:39:54

1	was reading.	11:39:56
2	Q. On page 405, which is page 11 of the PDF,	11:40:46
3	could you read the paragraph that starts with	11:40:51
4	"Patients were eligible for inclusion"?	11:40:53
5	A. Yes. Do you mind if I finish this? Just	11:40:55
6	one second.	11:40:58
7	Q. Sure.	11:40:58
8	A. Then I'll get to that.	11:40:59
9	Okay. What -- where did you want me to	11:41:12
10	read?	11:41:16
11	Q. On page 11 of 16, page 405 of the article,	11:41:16
12	the document. On the first column, there's a	11:41:21
13	paragraph under "Methods" --	11:41:25
14	A. Yes.	11:41:29
15	Q. -- that starts "Patients were eligible." If	11:41:29
16	you could read that paragraph.	11:41:34
17	A. "Patients were eligible." Oh, there we go.	11:41:38
18	Do you want me to read aloud or --	11:41:46
19	Q. No, just read it to yourself.	11:41:49
20	A. Okay.	11:42:12
21	Q. So do you agree that LoDoCo tested patients	11:42:12
22	who were clinically stable for at least six months?	11:42:18

1	A. Yes.	11:42:21
2	Q. And would you agree that LoDoCo shows that	11:42:21
3	daily administration of colchicine to myocardial	11:42:27
4	infarction patients could be beneficial?	11:42:32
5	MR. WILKERSON: Objection. Form.	11:42:35
6	A. Could be, yes. This is, again, not a	11:42:36
7	placebo-controlled study.	11:42:38
8	Q. Does it show efficacy after six months?	11:42:41
9	MR. WILKERSON: Objection to form.	11:42:46
10	A. Sorry. I don't understand. They didn't	11:42:47
11	give the drug in -- within six months. What they	11:42:49
12	did, they waited on these patients for six months	11:42:54
13	and then they gave it to them.	11:42:56
14	Q. Yes. So does it show efficacy for patients	11:42:59
15	for a time period starting with a prescription at	11:43:02
16	six months and going forward?	11:43:08
17	A. Right. So they had to have at least -- they	11:43:12
18	have to be at least six months away from their	11:43:16
19	angioplasty or myocardial infarction. So it could	11:43:19
20	be two years, it could be six months, it could be	11:43:21
21	four years.	11:43:24
22	So these are patients who have been away	11:43:25

1 from their angioplasty for at least six months, and 11:43:29
2 then they were randomized to colchicine or no 11:43:32
3 colchicine and they were followed for a period of 11:43:35
4 time. And the period of time they were followed is 11:43:36
5 shown in figure 2, and the subanalysis is shown in 11:43:39
6 figure 4. 11:43:48

7 Q. So based on figure 2, would you be 11:43:50
8 comfortable prescribing colchicine to a patient that 11:43:54
9 has been stable for six months? 11:43:57

10 A. I would say probably not based on this study 11:44:00
11 because this was not a placebo-controlled study. So 11:44:07
12 these are not as powerful as randomized 11:44:13
13 placebo-controlled studies. So I would not make a 11:44:18
14 clinical conclusion based on that. It's very 11:44:21
15 suggestive. It's very good study. But, you know, I 11:44:23
16 don't think my clinical practice would be -- would 11:44:28
17 change. 11:44:32

18 Q. Okay. So I'm handing you a copy of 11:44:32
19 Exhibit 1026. 11:44:36

20 (Exhibit 1026 was marked for 11:44:36
21 identification and was retained by counsel.) 11:44:38

22 Q. Are you familiar with this document? 11:44:38

1	A. I --	11:44:39
2	MR. WILKERSON: Is this marked anywhere?	11:44:52
3	MR. LAURENCE: It's -- if we can go off the	11:44:57
4	record for a moment.	11:44:59
5	THE VIDEOGRAPHER: Going off the record at	11:45:00
6	11:44 a.m.	11:45:01
7	(A short break was had.)	11:45:03
8	THE VIDEOGRAPHER: Going back on the record	11:45:47
9	at 11:45 a.m.	11:45:49
10	BY MR. LAURENCE:	11:45:50
11	Q. So the document I handed you is	11:45:51
12	Exhibit 1026. And as I mentioned while we were off	11:45:54
13	the record, the Bates number at the bottom did not	11:45:58
14	appear in the printed version for some reason, but	11:46:01
15	this is a correct version of Exhibit 1026.	11:46:04
16	Are you familiar with this document?	11:46:08
17	A. I can't remember if I've read this paper. I	11:46:10
18	can't say one way or the other. Sorry.	11:46:16
19	Q. Have you heard of LoDoCo 2?	11:46:18
20	A. Yes.	11:46:20
21	Q. So this is the paper that corresponds and is	11:46:20
22	known as LoDoCo 2.	11:46:24

1	Do you know what LoDoCo 2 is about?	11:46:26
2	A. Right. So LoDoCo 2 was with colchicine, I	11:46:28
3	believe, in patients with ST elevation MI, if I'm	11:46:37
4	not mistaken. I can't remember the details.	11:46:41
5	Q. Did it confirm the findings of the first	11:46:43
6	LoDoCo trial?	11:46:45
7	A. Yeah, from what I remember, I think it was	11:46:47
8	in a different group of patients. So yeah, so it	11:46:50
9	was -- it was supported. If you give me a copy of	11:46:56
10	LoDoCo 2, it would really help.	11:47:04
11	Q. So this document is LoDoCo 2.	11:47:05
12	A. I don't think so, no.	11:47:10
13	Q. It summarizes LoDoCo 2. Sorry.	11:47:12
14	A. Okay. Let me --	11:47:16
15	Q. Yes, that's correct. It's not LoDoCo 2 but	11:47:18
16	it summarizes LoDoCo 2. And if you could turn to	11:47:22
17	page 471.	11:47:26
18	A. Okay.	11:47:36
19	Q. Do you see the information listed about	11:47:36
20	COLCOT in table 2?	11:47:42
21	A. Yes.	11:47:44
22	Q. And then do you see the information on the	11:47:44

1	third row that relates to LoDoCo 2?	11:48:08
2	A. Yes.	11:48:13
3	Q. And do you see the sample size for LoDoCo 2,	11:48:13
4	5500?	11:48:20
5	A. Yes.	11:48:21
6	Q. And do you see that it's placebo controlled	11:48:21
7	in the next column?	11:48:26
8	A. Yes.	11:48:27
9	Q. So with this study of LoDoCo 2 being placebo	11:48:27
10	controlled, does that boost your confidence in the	11:48:37
11	effectiveness of colchicine as a therapy for a	11:48:40
12	patient that has been stable for at least six	11:48:46
13	months?	11:48:48
14	MR. WILKERSON: Objection. Form.	11:48:49
15	A. Well, again, I need to look at the LoDoCo 2.	11:48:50
16	I can't remember after how many months of	11:48:53
17	stabilization they were given colchicine. So to	11:48:56
18	answer your question, because you specifically ask	11:49:00
19	about six months, I need to look at the paper.	11:49:03
20	Q. Well, let's assume -- if we assume that	11:49:07
21	LoDoCo 2 tested for patients that were stable at	11:49:10
22	6 months, and combined with the knowledge that it's	11:49:14

1 placebo controlled, would that suffice for you to 11:49:18
 2 feel comfortable saying that there's a therapeutic 11:49:23
 3 benefit for patients that have been stable for at 11:49:26
 4 least six months? 11:49:29

5 MR. WILKERSON: Objection. Form. 11:49:31

6 A. What you're saying is that, if LoDoCo 2 11:49:34
 7 randomized patients who had been stable for at least 11:49:39
 8 six months since their myocardial infarction and 11:49:42
 9 angioplasty and there was benefit of chronic 11:49:44
 10 treatment with colchicine, would I feel comfortable 11:49:48
 11 to start colchicine after six months in terms of 11:49:53
 12 prevention of coronary events? Yes, it would be 11:49:58
 13 supportive that that treatment is beneficial in 11:50:03
 14 these patients. 11:50:08

15 Q. Okay. So at what time period earlier than 11:50:09
 16 six months would you not be comfortable in 11:50:28
 17 prescribing colchicine? 11:50:30

18 MR. WILKERSON: Objection. Form. 11:50:35

19 Q. Would you expect that it would be 11:50:36
 20 ineffective at five months? 11:50:40

21 MR. WILKERSON: Same objection. 11:50:42

22 A. Well, based on the data I have right now, my 11:50:42

1 conclusion is that, if somebody comes to the 11:50:46
2 hospital and they have myocardial infarction and 11:50:49
3 they get angioplasty, it's a good practice or there 11:50:51
4 is data to support that, if you start colchicine 11:50:57
5 within 3 days, it would have beneficial effects. 11:51:01

6 Now, we also have data -- again, I haven't 11:51:04
7 seen the paper so I'm taking your word for it -- 11:51:07
8 that, if someone has been stabilized for at least 11:51:11
9 six months and they had their myocardial infarction 11:51:13
10 and angioplasty at least six months earlier, you can 11:51:16
11 also start that group of patients on colchicine. 11:51:22

12 You're asking me about five months. All I 11:51:23
13 can tell you is that those patients who were started 11:51:26
14 after 8 days in the hospital or after 8 days from 11:51:30
15 their myocardial infarction, based on COLCOT and 11:51:34
16 subanalysis that was done by Dr. B, that didn't show 11:51:38
17 benefit. So anywhere between 4 days and six months, 11:51:41
18 I don't have enough data to tell you when to start 11:51:45
19 on those patients. But everything else is based on 11:51:48
20 clinic -- randomized clinical trials, and everything 11:51:51
21 else I told you is based on that. So ... 11:51:55

22 Q. So is it accurate to say you're comfortable 11:51:58

1 with prescribing colchicine within the 0 to 3-day
2 period and then after six months of stability, but
3 the periods in between there are the question mark
4 for you?

5 MR. WILKERSON: Objection to form.

6 A. Well, what I would say is that first, I have
7 to wait for the FDA approval, right? So if the FDA
8 approves this drug, they're probably gonna also
9 provide some additional information.

10 Now, do we follow everything that the FDA
11 puts on their label? No. I mean, physicians, we
12 make our decisions, right? Our decision. And we
13 don't give medications on-label based on the label
14 all the time. We give medications off-label all the
15 time. So based on the clinical evidence I have
16 right now, I believe that -- or the evidence
17 suggests that within 3 days after MI and after
18 angioplasty -- and, again, I take your word for it.
19 I haven't looked at the LoDoCo 2 carefully, but even
20 after six months, those are the groups of patients
21 where randomized clinical trials are supported by
22 starting colchicine.

1 Now, one other thing I want to mention is 11:53:20
2 that LoDoCo 2 did not include a loading dose. Their 11:53:23
3 patent doesn't exclude a loading dose. The patent 11:53:30
4 for LoDoCo 1, I should say. And -- but the other 11:53:33
5 patent specifically talked about excluding loading 11:53:37
6 dose. 11:53:41

7 Now, does it play a role in my practice? 11:53:41
8 You know, patents don't, but, you know, the clinical 11:53:44
9 studies do. 11:53:47

10 Q. And are you only comfortable prescribing a 11:53:48
11 medication if it's based on a randomized study? 11:53:52

12 MR. WILKERSON: Objection to form. 11:53:57

13 A. Again, most of our practice is based on 11:53:59
14 randomized clinical trials. But not everything. As 11:54:02
15 I said earlier, I -- we have done -- you know, we 11:54:05
16 have decided on how to give a medication based on 11:54:10
17 post hoc analysis. We have given medications based 11:54:14
18 on nonrandomized clinical trials. So not everything 11:54:18
19 is based on randomized clinical trials. 11:54:24

20 Q. Well, which one is more compelling, LoDoCo 11:54:26
21 plus LoDoCo 2 in establishing efficacy at six 11:54:30
22 months, or post hoc analysis of the 0 to 3 days? 11:54:33

1	MR. WILKERSON: Objection. Form.	11:54:37
2	A. I don't know if I'm going to make a	11:54:39
3	conclusion based on which one is more reliable. All	11:54:45
4	I can tell you is that COLCOT is a very good study,	11:54:49
5	and it, basically, tells you if you start colchicine	11:54:54
6	without a loading dose within 30 days is beneficial.	11:54:58
7	Now, they looked at the numbers, and it looks like	11:55:02
8	it's better if you start within 3 days. That's	11:55:06
9	where you get the maximal effect. I believe that.	11:55:09
10	I would follow that practice.	11:55:11
11	Now, for LoDoCo 2, again, if this is 5500	11:55:14
12	and the study was very positive, yes, I would say I	11:55:21
13	would start it in patients who have been stable for	11:55:24
14	more than six months, I would give them the	11:55:27
15	medication too.	11:55:30
16	Q. But based on COLCOT, which established	11:55:30
17	effectiveness for patients that have been stable for	11:55:35
18	30 days with a myocardial infarction, would you be	11:55:40
19	comfortable then prescribing colchicine at low doses	11:55:44
20	for patients that have been stable at 30 days based	11:55:48
21	on COLCOT?	11:55:52
22	MR. WILKERSON: Objection. Form.	11:55:53

1 A. So what I would do, my primary focus or my
2 primary goal would be to start medication within
3 three days because that's where the benefit was
4 shown. And that's what I would do. Now, if they
5 come at 30 days, I would talk to them probably, and
6 I'd say, there is not enough evidence to support
7 that giving you medication at this point would be
8 beneficial. I can start you on it. The clinical
9 trials show that if you come back after six months,
10 it may help you at that time. But at 30 days, the
11 studies are not supportive.

12 Q. So COLCOT established that colchicine worked
13 within 30 days; isn't that correct?

14 A. Correct.

15 Q. So based on COLCOT, you'd be comfortable
16 prescribing it within the 30-day time period?

17 A. Again, I would have that conversation with
18 my patient and say, there is not enough evidence
19 that it would help you if it has been 30 days away
20 from their myocardial infarction and angioplasty.
21 My goal will be to start it while the patient is in
22 the hospital in the first 3 days. So there would be

1 very few patients, at least under my care, who would 11:57:14
2 not get colchicine in the first three days. And I 11:57:18
3 think based on the overall studies we have, very few 11:57:22
4 cardiologists would not start patients on colchicine 11:57:26
5 in the first 3 days, based on what we have, and just 11:57:29
6 wait until they go, you know, to clinic and then 11:57:32
7 they start it. So I think there will be very few 11:57:34
8 patients who would fall off, you know, this time 11:57:37
9 period and not get started within three days. 11:57:40

10 Q. So do you see a contradiction between what 11:57:55
11 COLCOT established and what Dr. Bouabdallaoui's 11:58:00
12 paper indicates? 11:58:05

13 MR. WILKERSON: Objection to form. 11:58:07

14 A. No. I wouldn't say there's 11:58:09
15 contraindication. I would say that Dr. B's paper 11:58:12
16 refined the time period better. You know, they 11:58:15
17 looked at a long time period. But that doesn't mean 11:58:19
18 that every patient in that time period got the same 11:58:22
19 benefit. That's why this subanalysis was done, and 11:58:26
20 that's why Dr. B's paper is very helpful. It's very 11:58:30
21 helpful. It, basically, tells us that you have to 11:58:34
22 start colchicine early in -- for your patients. And 11:58:36

1	that's what we are gonna be doing as cardiologists.	11:58:41
2	Q. And so the COLCOT within 30 days,	11:58:45
3	numerically, that includes within 3 days; correct?	11:58:49
4	A. Correct.	11:58:52
5	Q. If you knew that there's a therapeutic	11:58:53
6	benefit to treating within 30 days, would you be	11:58:55
7	inclined to test, in your lab, the results for	11:58:59
8	patients that have a myocardial infarction and you	11:59:05
9	want to look at periods less than 30 days?	11:59:12
10	MR. WILKERSON: Objection to form.	11:59:14
11	A. I'm sorry. I don't understand the question.	11:59:15
12	First of all, I don't do these studies in my	11:59:21
13	lab. But if you're asking, do I want to look at	11:59:24
14	what time period would be more beneficial, I already	11:59:27
15	have the answer. That was in Dr. B's paper. And	11:59:29
16	that's the point I'm trying to emphasize here. That	11:59:34
17	cardiologists, we have the data. Now we know. And	11:59:37
18	that's why I think this paper is a really big step	11:59:41
19	forward in our practice if this drug gets approved	11:59:45
20	by the FDA, that we need to be aggressive. We need	11:59:49
21	to start these patients on colchicine before they	11:59:53
22	are discharged within the first 3 days.	11:59:56

1 So what I will probably do if this drug gets
2 approved by the FDA is I'm gonna tell my residents,
3 as soon as they are -- you know, the patient goes to
4 the cath lab and they come back, I would say this
5 patient should be on statins, they should be on beta
6 blockers, their blood pressure should be controlled,
7 their diabetes should be controlled, their -- you
8 know, cholesterol should be controlled, they should
9 also be on colchicine while they are in the
10 hospital. So that's how this is gonna change our
11 practice.

11:59:57

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12 I'm not gonna wait and say, well, go to the
13 patient and say, well, when you are discharged, make
14 sure you see the nurse practitioner, and make sure
15 you start this drug colchicine within the first
16 30 days.

12:00:28

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17 Q. It's easier to treat a patient while they're
18 in the hospital; right?

12:00:41

12:00:43

19 A. That's not the only reason. Yes, it is
20 easier to start in the hospital. But the point I'm
21 making is that I'm not gonna base my practice on the
22 results of COLCOT. I'm gonna base it on what

12:00:44

12:00:46

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12:00:52

1 Dr. B's paper showed, and I'm gonna try to get my
2 trainees to start the medication within 3 days while
3 they are in the hospital.

4 Q. But that's based on information you have
5 now.

6 A. Right.

7 Q. If you were a person of ordinary skill in
8 the art after the COLCOT study came out and you saw
9 that there was a beneficial use of colchicine for
10 patients that had a myocardial infarction and
11 they've been stable for 30 days, you know that it's
12 easier to treat patients while they're in the
13 hospital, wouldn't you be inclined to treat them at
14 any time period within 30 days?

15 MR. WILKERSON: Objection to form.

16 A. Just based on COLCOT?

17 Q. Uh-huh.

18 A. Well, COLCOT says any time you start within
19 30 days, it has -- in those patients, there was
20 beneficial effects. So if it was only on that, yes.
21 But again, that's why this other paper really is a
22 major step forward because it tells us that you

1 gotta treat these patients in the acute phase. And
2 that's probably because that's where the
3 inflammatory process is very -- is very active.

4 So what happens is that the heart gets
5 damaged. The immune cells, which are basically the
6 soldiers in our body, they say something has been
7 damaged. We've gotta go and repair it. And we
8 think that this repair process is actually a good
9 thing. And there are a lot of good things that
10 happen when this repair process goes to the heart to
11 do its job.

12 But it also does bad things. So it looks
13 like if you inhibit that -- you know, that
14 inflammatory process is beneficial to these
15 patients, as if you start it as early as possible.

16 Q. So when do you think the FDA will approve
17 colchicine for cardiovascular disease?

18 MR. WILKERSON: Objection. Form.

19 A. When will they approve it? I have no idea.

20 Q. If you could go to Claim 27 of the
21 '063 patent?

22 A. Okay.

1 Q. Do you see that it recites that [As read]
2 the method comprising initiating the administration
3 of colchicine at a daily low dose to the patient
4 within about 30 days of an MI.

5 A. Yes.

6 Q. If you gave a patient who has experienced a
7 myocardial infarction a daily low dose of colchicine
8 starting within 30 days of the myocardial
9 infarction, will that reduce the risk of stroke in
10 the patient?

11 MR. WILKERSON: Objection. Form.

12 A. Right. So in COLCOT, one of the factors or
13 one of the end points that drove the primary end
14 point to be significant was a stroke in the first
15 30 days. So a stroke was significantly different
16 between the two groups. So based on that, yes, if
17 it is started within the first 30 days -- if
18 colchicine is started within the first 30 days, it
19 would reduce the risk of stroke in patients after
20 MI.

21 Q. And so that's true today, and it was true
22 ten years ago; is that correct?

1	MR. WILKERSON: Objection to form.	12:04:52
2	A. Sorry. I'm not understanding the question.	12:04:53
3	Q. I'm sorry.	12:04:56
4	When the COLCOT study was published, was	12:04:56
5	that true then?	12:04:59
6	A. In terms of the reduction in stroke? The	12:05:04
7	study suggested yes, that there's a reduction in	12:05:07
8	stroke.	12:05:12
9	Q. So if you could, describe the COLCOT study	12:05:15
10	in your own words.	12:05:19
11	A. Sure. So these patients who had myocardial	12:05:20
12	infarction and they underwent coronary intervention,	12:05:27
13	within the first 30 days after their coronary	12:05:32
14	intervention, they were started on colchicine	12:05:36
15	.5-milligram per day. And without a loading dose.	12:05:39
16	And they were followed for a number of years. And	12:05:46
17	they were -- they looked at the primary end point of	12:05:49
18	stroke, I believe recurring revascularization and	12:05:54
19	death from cardiovascular disease. I can't remember	12:05:59
20	all the primary end points, but there was a	12:06:01
21	composite primary end point they looked at. And	12:06:04
22	there was a significant reduction in that composite	12:06:07

1 end point when patients were started on colchicine 12:06:10

2 within the first 30 days. 12:06:15

3 Q. Do you know whether the COLCOT study was 12:06:27

4 designed in advance to test any hypothesis related 12:06:29

5 to time-to-treatment initiation? 12:06:38

6 A. I don't think that was one of the factors 12:06:41

7 that went into the design of this study. 12:06:43

8 Q. And in your first declaration, in 12:06:47

9 paragraph 25, you state that the COLCOT trial did 12:07:12

10 not investigate the effect of low-dose colchicine on 12:07:25

11 patients unless they were stabilized; is that 12:07:28

12 correct? 12:07:36

13 A. Yes. 12:07:36

14 Q. And what period of time do you consider that 12:07:36

15 to include? 12:07:39

16 A. Well, that means they had gone to the cath 12:07:48

17 lab. They were -- they didn't have evidence of 12:07:50

18 anything acute going on because their vessel was 12:07:54

19 opened up, and they were taken back to the room, and 12:07:59

20 they were stable enough to start taking their other 12:08:02

21 medications. 12:08:05

22 Q. And when you say "stable," what do you mean 12:08:08

1	by that?	12:08:12
2	A. That means they were hemodynamically stable	12:08:12
3	and they didn't have any active thrombotic event	12:08:18
4	going on in their body.	12:08:23
5	Q. And at what point are patients discharged	12:08:24
6	from the hospital?	12:08:26
7	A. Right. So, again, as I said earlier, the	12:08:27
8	majority of these patients are discharged within the	12:08:30
9	first two to three days.	12:08:33
10	Q. And in paragraph 27, you state that the '285	12:08:36
11	application, which is the application from which the	12:08:44
12	'063 patent issued, you state that the '285	12:08:49
13	application included additional information from the	12:08:54
14	COLCOT data that was consistent with the two	12:08:57
15	previous provisional applications.	12:09:00
16	Could you elaborate on what that additional	12:09:02
17	information is?	12:09:04
18	A. I can't remember. Sorry. I'd have to look	12:09:15
19	at the dose in detail. Sorry.	12:09:18
20	Q. Is the additional information the 0-to-3-day	12:09:24
21	time period and the 4-to-7-day TTI?	12:09:30
22	MR. WILKERSON: Object to form.	12:09:32

1 A. Probably. I can't remember. Again, sorry. 12:09:34

2 Q. So what factors do you consider when 12:10:19

3 deciding to have a loading dose and to not have a 12:10:23

4 loading dose for any general medication, not 12:10:30

5 colchicine specifically but for different types of 12:10:32

6 medication? 12:10:34

7 MR. WILKERSON: Objection. Form. 12:10:34

8 A. I don't think we can make a general 12:10:35

9 statement regarding a loading dose for different 12:10:38

10 drugs. But, generally, we think of loading dose 12:10:41

11 when we think in different terms. For example, for 12:10:45

12 a drug called amiodarone, we give a loading dose, 12:10:52

13 and that's the drug we use for cardiac arrhythmias, 12:10:56

14 including atrial fibrillation. And the reason is 12:11:02

15 that, if you give amiodarone to your patients, it 12:11:05

16 almost always goes to the fat tissue so your blood 12:11:09

17 doesn't see much of that. So you have to give a lot 12:11:13

18 of amiodarone to basically saturate the fat tissue 12:11:16

19 first and then it goes to the level or therapeutic 12:11:19

20 level in the blood. So that's one reason for giving 12:11:22

21 a loading dose. 12:11:25

22 Another reason would be because the -- there 12:11:27

1 is an active process going on that needs to be 12:11:30
2 targeted very effectively, and a clear example of 12:11:33
3 that would be somebody who comes in with myocardial 12:11:37
4 infarction and they likely have a thrombus in their 12:11:41
5 coronary vessel, so we give 600 milligrams of 12:11:46
6 Plavix. So we pre-load them to make sure that that 12:11:49
7 thrombus is effectively targeted. So that's another 12:11:54
8 example of the reason to give a loading dose. 12:11:58

9 In terms of inflammation, you know, for 12:12:01
10 almost every disease where we gave -- where we give 12:12:04
11 colchicine, you want to treat the inflammation very 12:12:09
12 effectively. So you give a loading dose. 12:12:12

13 So it's, again, I think this COLCOT study, 12:12:15
14 and what we learn afterwards from Dr. B's paper, is 12:12:21
15 very helpful, is extremely helpful because, you 12:12:24
16 know, if I have a patient with pericarditis, I tell 12:12:30
17 my residents and my medical students, make sure you 12:12:34
18 give a loading dose to these patients. So this was 12:12:38
19 common practice to give a loading dose of 12:12:41
20 colchicine. And here, we learned that, in patients 12:12:43
21 who have myocardial infarction, it's not needed. As 12:12:45
22 long as you start early, it is beneficial. 12:12:48

1	So sorry, that was a long answer to your	12:12:51
2	question, but there are different factors that go	12:12:54
3	into the consideration why to give a loading dose.	12:12:57
4	Q. But do you consider it standard procedure to	12:12:59
5	add a loading dose when none is specified?	12:13:03
6	MR. WILKERSON: Object to form.	12:13:07
7	A. Sorry. I don't understand the question. If	12:13:09
8	the loading dose is not specified.	12:13:11
9	Q. If a medication is not understood to have	12:13:13
10	been tested with a loading dose, would you just add	12:13:20
11	a loading dose on your own?	12:13:24
12	A. No. I mean, the majority of the medications	12:13:28
13	we give to our patients is one dose, and you just	12:13:31
14	give it to your patients and, you know, to make sure	12:13:35
15	that the therapeutic effect of the drug is within	12:13:41
16	the therapeutic range of the drug.	12:13:44
17	So a lot of pharmacological studies go into	12:13:46
18	it. You know, we do pharmacokinetics and	12:13:50
19	pharmacodynamics on these drugs. And if there is a	12:13:58
20	reason to give a loading dose, it is based on	12:14:00
21	pharmacodynamics -- or pharmacokinetics of the drug.	12:14:03
22	And, again, an example of that was amiodarone. It	12:14:07

1 doesn't go into the therapeutic range unless you 12:14:07

2 load the patient with amiodarone. 12:14:10

3 Q. And if nothing like that has been 12:14:10

4 established, would you give a patient a medication 12:14:12

5 with a loading dose? 12:14:15

6 A. No. 12:14:16

7 MR. WILKERSON: Object to form. 12:14:16

8 A. In fact, I have some patients who come to me 12:14:17

9 and they say, "Well, you know, sometimes my blood 12:14:20

10 pressure is high so I take two of my pills." I 12:14:24

11 discourage them. 12:14:27

12 I say, "That's not how medications work. We 12:14:28

13 have a therapeutic range. You've gotta take your 12:14:30

14 medications on a regular basis." 12:14:35

15 Q. So it's safe to say that, if the only active 12:14:40

16 agent in the clinical protocol isn't described with 12:14:46

17 a loading dose, you wouldn't, on your own, tell a 12:14:49

18 patient to use a larger amount as a loading dose to 12:14:53

19 kick things off? 12:14:57

20 MR. WILKERSON: Objection. Form. 12:14:59

21 A. I can't think of an example of any 12:15:00

22 medications where I've done that. I don't see any 12:15:11

1 reason why you would do that. 12:15:14

2 Q. And if you were participating in a clinical 12:15:15

3 study as a treating physician, would you add a 12:15:18

4 loading dose of the active agent if the clinical 12:15:21

5 study did not explicitly call for a loading dose? 12:15:24

6 A. So if I was one of the investigators on a 12:15:27

7 clinical study, no, I would follow the protocol for 12:15:31

8 the clinical study. 12:15:35

9 Q. And what would the FDA do if you deviated 12:15:36

10 from the protocol for the clinical study? 12:15:38

11 A. I don't know what the FDA would do, but the 12:15:42

12 clinical protocol has to be followed. And the 12:15:45

13 clinical protocol usually is reviewed by the FDA 12:15:48

14 before a Phase 3 clinical study is done. 12:15:52

15 Q. And would the patient's data be included in 12:15:58

16 the study or need to be removed, if you added a 12:16:02

17 loading dose on your own outside of the boundaries 12:16:04

18 of the protocol? 12:16:09

19 A. If the principal investigator thinks that 12:16:13

20 that's deviation from the protocol, I think they 12:16:16

21 would remove the patient. 12:16:19

22 Q. And you indicated in your second declaration 12:16:37

1 that you serve as the deputy editor of the "Journal
2 of Clinical Investigation."

3 Do you have any other leadership role in
4 that organization, in the American Society For
5 Clinical Investigation?

6 A. Yes. Well, I was -- you know, it's an honor
7 society. So if you get into it, it's basically, you
8 know, makes it to the university newspapers. And
9 there's an age limit.

10 So I was inducted in 2012. And I served as
11 the treasurer of the society for two years. I was
12 on the council. And then I served as the president
13 of the society in 2021. I was -- I think I was the
14 first president of the ASCI in the history of
15 Northwestern, so that was -- you know, that was --
16 you know, I was humbled by that appointment. So ...

17 MR. LAURENCE: Why don't we stop there for
18 lunch.

19 THE VIDEOGRAPHER: Going off the record at
20 12:16 p.m.

21 (A short break was had.)

22 THE VIDEOGRAPHER: Going back on the record

1	at 1:09 p.m.	13:10:09
2	BY MR. LAURENCE:	13:10:15
3	Q. Dr. Ardehali, we talked about some	13:10:17
4	characteristics in the Bouabdallaoui study.	13:10:18
5	Would you expect a patient to recover better	13:10:30
6	or more easily if they did not have hypertension?	13:10:39
7	MR. WILKERSON: Object to form.	13:10:43
8	A. Well, hypertension is a risk factor for	13:10:44
9	cardiovascular disease, and it's also -- you know,	13:10:48
10	it's one of the risk factors that we want to reduce	13:10:56
11	in our patients.	13:11:00
12	Q. So if a patient doesn't have hypertension,	13:11:01
13	they're more likely to recover and become a healthy	13:11:03
14	person after an MI?	13:11:18
15	MR. WILKERSON: Objection to form.	13:11:20
16	A. That really depends on how the patient is	13:11:21
17	treated. If you get their blood pressure under	13:11:24
18	control and you give them good medications, I think	13:11:28
19	the risk goes down significantly.	13:11:31
20	Q. And would you expect a patient that has no	13:11:34
21	diabetes to lead to a better outcome?	13:11:42
22	MR. WILKERSON: Objection to form.	13:11:51

1 A. Again, if they are treated aggressively, the
2 risk goes down significantly. Now, it has been
3 studied, you know, all of these treatments have been
4 studied in general population. However, whether or
5 not, post MI, reducing, you know, the incidence of
6 hypertension by treating with medications, whether
7 or not that would reduce it to the level of someone
8 who doesn't have hypertension, I would say probably
9 yes. But I don't think there are any clinical
10 studies that have looked at that specifically. Same
11 thing with diabetes.

12 Q. So if a patient has had no prior MI, would
13 that characteristic predictably lead to a better
14 outcome.

15 MR. WILKERSON: Objection. Form.

16 A. I'm sorry. I didn't follow the question.

17 Q. If a patient has not had a prior MI --

18 A. Right.

19 Q. -- would that characteristic lead to a
20 better outcome?

21 MR. WILKERSON: Same objection.

22 A. What characteristic?

1 Q. Not having had an MI. 13:12:57

2 A. Right. So having an MI is a risk factor for 13:13:00

3 a second MI. 13:13:02

4 Q. Okay. And if you've had no prior CABG, 13:13:04

5 would that predictably lead to a better outcome? 13:13:08

6 MR. WILKERSON: Object to form. 13:13:11

7 A. Depends on who you compare it to. I would 13:13:17

8 say, if you have an underlying coronary disease that 13:13:22

9 required CABG, of course, you are at a high risk of 13:13:24

10 having worse events compared to someone who is 13:13:29

11 younger and doesn't have coronary disease. But I 13:13:32

12 think CABG is just a procedure that shows that the 13:13:35

13 patient had coronary disease. 13:13:38

14 Q. Well, if you had a prior heart failure, is 13:13:40

15 that a characteristic that would predictably lead to 13:13:44

16 a better outcome? 13:13:48

17 A. I agree with heart failure. If you have 13:13:50

18 heart failure, you are at higher risk of having 13:13:53

19 worse outcome. 13:13:56

20 Q. And how about no prior stroke? Would you 13:13:59

21 expect that characteristic to lead to a better 13:14:06

22 outcome? 13:14:08

1 A. I can't say for sure. I would say probably 13:14:17
2 yes. 13:14:20

3 Q. How about having PCI to treat the current 13:14:20
4 MI? 13:14:23

5 A. Well, in general, if you have an MI, you are 13:14:25
6 at higher risk of having another MI. 13:14:29

7 Q. And then how about quitting smoking? 13:14:36

8 A. So if you have a history of smoking, you are 13:14:41
9 at high risk of cardiovascular events. If you quit 13:14:44
10 smoking, your risk doesn't go to zero but it goes 13:14:48
11 significantly lower. 13:14:51

12 Q. And then how about stabilizing sooner after 13:14:55
13 the current MI? 13:14:58

14 MR. WILKERSON: Objection to form. 13:15:04

15 A. Yeah. To be honest, I don't understand the 13:15:06
16 question. Compared to what? 13:15:09

17 Q. Well, is it -- if you stabilize earlier as 13:15:10
18 opposed to later, is that a characteristic that 13:15:14
19 would lead to a better outcome? 13:15:17

20 MR. WILKERSON: Objection. Form. 13:15:21

21 A. It depends on why you would stabilize later. 13:15:25
22 That, to me, suggests that MI was more complicated. 13:15:28

1 And that probably suggests that there was more going 13:15:33
2 on in terms of the underlying disease. So probably 13:15:35
3 yes, but again, I need more information to give a 13:15:40
4 definitive answer to that question. 13:15:43

5 Q. Okay. Could you generalize -- based on 13:15:45
6 these characteristics that we've talked about, can 13:15:51
7 you make any generalizations about data based on 13:15:55
8 patients that have had hypertension, diabetes, a 13:16:02
9 prior MI, prior CABG, prior heart failure, are those 13:16:05
10 types of things that would -- if a patient has those 13:16:13
11 characteristics, would they likely have a better 13:16:19
12 outcome than patients that have diabetes or a prior 13:16:29
13 MI or prior CABG, prior heart failure? 13:16:34

14 MR. WILKERSON: Objection. Form. 13:16:37

15 A. Well in terms of hypertension and diabetes, 13:16:38
16 I would say that really depends on whether or not 13:16:41
17 those are treated well. And so that's something, 13:16:43
18 yes, I would take into consideration. 13:16:52

19 Now, if you are talking about prior MI, if 13:16:55
20 the patient has an MI, the risk goes up 13:16:57
21 significantly. So if you are talking about patients 13:17:02
22 who were included in Dr. B's study, they all had MI. 13:17:05

1 Right? Because they have to have an MI to be 13:17:10
2 included. So they are all high risk. And having a 13:17:12
3 prior MI doesn't increase your risk anymore. You 13:17:15
4 just had an MI so your risk is as high as somebody 13:17:19
5 who had an MI before. 13:17:23

6 Q. Okay. Let me hand you Exhibit 1006, and 13:17:32
7 this is another exhibit where the Bates numbering 13:17:42
8 disappeared, but this is a correct version of 13:17:46
9 Exhibit 1006. 13:17:51

10 MR. LAURENCE: Let's go off the record for a 13:18:19
11 minute. 13:18:21

12 THE VIDEOGRAPHER: Going off the record at 13:18:21
13 1:17 p.m. 13:18:23

14 (A short break was had.) 13:18:23

15 THE VIDEOGRAPHER: Going back on the record 13:19:37
16 at 1:19 p.m. 13:19:39

17 BY MR. LAURENCE: 13:19:42

18 Q. I apologize. I meant to hand you 13:19:42
19 Exhibit 1007. 13:19:45

20 (Exhibit 1007 was marked for 13:19:45
21 identification and was retained by counsel.) 13:19:48

22 Q. This is U.S. Patent 10,206,891 issued to 13:19:48

1	Nidorf.	13:19:54
2	Are you familiar with this patent?	13:19:56
3	A. Yes.	13:20:08
4	Q. So this is the patent to Mr. Nidorf who	13:20:08
5	authored the LoDoCo protocol; is that correct?	13:20:18
6	A. I'm sorry. This thing is making some noise.	13:20:22
7	I don't know if this is -- this should be doing it.	13:20:25
8	It stopped making noise. It's okay now.	13:20:31
9	I'm sorry. What was the question?	13:20:40
10	Q. Are you familiar with this patent?	13:20:42
11	A. Yes.	13:20:46
12	Q. And is it correct that this protocol	13:20:46
13	described in the Nidorf patent is silent about a	13:20:54
14	loading dose?	13:20:57
15	A. I have to look at the protocol more	13:21:19
16	carefully. But from what I remember, I think I	13:21:23
17	agree with that, yes.	13:21:26
18	Q. Okay. And I'm handing you a copy of	13:21:27
19	Exhibit 2010.	13:21:46
20	(Exhibit 2010 was marked for	13:21:46
21	identification and was retained by counsel.)	13:21:50
22	Q. And if you could turn in your first	13:21:50

1	declaration --	13:21:58
2	A. That's what I was talking about.	13:22:08
3	Q. -- to paragraph 38 on page 17.	13:22:15
4	A. Okay.	13:22:29
5	Q. You refer to "some studies" in that first	13:22:29
6	line of paragraph 38 and then cite to Exhibit 2010;	13:22:33
7	is that correct? In footnote 34?	13:22:48
8	A. Yes.	13:22:49
9	Q. Is Exhibit 2010 the studies you are	13:22:50
10	referring to?	13:22:54
11	A. I believe so, yes.	13:22:56
12	Q. What does Exhibit 2010 relate to?	13:22:57
13	A. It's high versus low dosing of oral	13:23:10
14	colchicine for early acute gout flare.	13:23:12
15	Q. Okay.	13:23:15
16	THE WITNESS: Can we ask them to mute? This	13:23:18
17	is very -- okay.	13:23:20
18	Q. Can you read the second sentence of	13:23:24
19	paragraph 39 in your declaration?	13:23:26
20	A. [As read] A POSA would therefore understand	13:23:30
21	that the long-term of stability would not have	13:23:33
22	reasonably expected that one could remove a loading	13:23:36

1 dose from a patient shortly after their MI because 13:23:40
2 the inflammation would be expected to be much more 13:23:43
3 severe. 13:23:46

4 Q. And what does that sentence mean? 13:23:48

5 A. So that means after an MI -- and this is 13:23:53
6 something I was referring to this morning -- there 13:23:56
7 is a systemic inflammation, and there's also 13:24:01
8 inflammation that occurs in the heart. And that's 13:24:04
9 the time when there is -- it's more prominent, the 13:24:08
10 inflammation during that time is more prominent and 13:24:15
11 more severe. So this is the time you would expect 13:24:18
12 that a higher dose of colchicine would be more 13:24:20
13 effective. So a POSA would have thought that this 13:24:24
14 is the time you should actually give a higher dose 13:24:26
15 of colchicine to these patients. 13:24:29

16 MR. LAURENCE: If those who are remote are 13:24:35
17 not muted -- excuse me. Those who are remote, if 13:24:38
18 you could check your microphones to make sure you're 13:24:46
19 muted, there's some sound coming through. 13:24:49

20 BY MR. LAURENCE: 13:25:36

21 Q. In the COLCOT protocol, which was initiated 13:25:37
22 within 30 days of a myocardial infarction, when do 13:25:40

1 you believe that each patient started the treatment, 13:25:44

2 and who dictated when they started the treatment? 13:25:47

3 MR. WILKERSON: Objection. Form. 13:25:49

4 A. Are you asking me when within those -- that 13:25:51

5 30-day period? 13:25:55

6 Q. Yes. 13:25:57

7 A. So we have some indication of how many of 13:26:00

8 these patients were started in 0 to 3 days versus 4 13:26:06

9 to 7 days and more than 8 days. But how many 13:26:10

10 patients were started in each one of those days, 13:26:15

11 that, we need more information, and I couldn't find 13:26:21

12 any information with those, you know, specific days 13:26:23

13 divided into 30 different categories. And who 13:26:28

14 decided when to start those medications would be the 13:26:32

15 group who recruited the patient. So the protocol 13:26:36

16 said within 30 days. And the physician or the team 13:26:41

17 that recruited the patient, they decided at what 13:26:47

18 point the patient should be started. 13:26:50

19 Q. And what role would the treating physician 13:26:52

20 have in that decision-making? 13:26:54

21 A. Well, the treating physician could be the 13:26:58

22 physician who recruited the patient, and so they 13:27:01

1 would be the ones who would decide. 13:27:03

2 Q. And what do you think was the typical 13:27:07

3 scenario? 13:27:09

4 MR. WILKERSON: Objection to form. 13:27:10

5 A. The typical scenario would be that the team 13:27:12

6 that is involved in the patient recruitment would be 13:27:18

7 called to make sure that the patient is qualified to 13:27:21

8 be included in the study. And after the decision 13:27:24

9 was made to start the patient on -- or to be -- to 13:27:29

10 include the patient in the study, they decide -- 13:27:35

11 they would decide when to start the medication. And 13:27:38

12 somebody would tell them what kind of medication the 13:27:41

13 patient should be given, either placebo or 13:27:44

14 colchicine, but they would be blinded to the 13:27:48

15 treatment they are getting. 13:27:50

16 Q. So assuming FDA approval, does it make sense 13:27:51

17 to start as soon as possible with colchicine 13:28:01

18 treatment? 13:28:04

19 MR. WILKERSON: Objection to form. 13:28:05

20 A. I'm sorry. What was the question? 13:28:07

21 Q. Assuming FDA approval, does it make sense to 13:28:08

22 start treatment as soon as possible for a patient? 13:28:12

1 MR. WILKERSON: Same objection. 13:28:15

2 A. Yes, within the first 3 days. Yes. 13:28:16

3 Q. And we've talked about these different time 13:28:18

4 periods. We've talked about COLCOT testing within 13:28:28

5 30 days. And we talked about LoDoCo starting within 13:28:34

6 six months. 13:28:38

7 Is there any biological reason that you 13:28:40

8 wouldn't expect colchicine to be effective as a 13:28:45

9 treatment for a time period of 30 days to six 13:28:50

10 months? 13:28:53

11 MR. WILKERSON: Objection. Form. 13:28:54

12 A. Right. So first of all, COLCOT wasn't 13:28:55

13 within six months. It was after six months. 13:28:58

14 Q. After six months, yes. 13:29:00

15 A. Right. So is there any biological reason 13:29:02

16 why it wouldn't be effective between 30 days and six 13:29:04

17 months? 13:29:09

18 Q. Yes. 13:29:09

19 A. I would say the most likely time that it 13:29:10

20 would be effective would be likely shortly after the 13:29:13

21 myocardial infarction. That's the time that we 13:29:17

22 know, based on these studies, that the drug has the 13:29:20

1 highest efficacy. But whether or not there would be 13:29:22
2 some residual effects during that time we can't 13:29:25
3 tell, based on the studies we have right now. And 13:29:31
4 that would require additional studies. 13:29:33

5 Would I start a patient when they're four 13:29:39
6 months away from a myocardial infarction? As I said 13:29:42
7 earlier, that's a conversation I would have with my 13:29:45
8 patients if this drug gets approved. And I would 13:29:48
9 say that this drug -- this is the data that is out 13:29:51
10 there, and I may encourage my patients, if 13:29:53
11 additional studies come along by that time, to take 13:29:56
12 the medication. Or I may be agnostic to the 13:30:00
13 treatment as a -- it's up to you. I would probably 13:30:03
14 not do it until -- you know, when you hit the 13:30:07
15 six-month mark, based on the clinical studies we 13:30:11
16 have. 13:30:14

17 But I guess let me step back. You were 13:30:15
18 asking me if there is a biological reason that it 13:30:17
19 wouldn't work, right? 13:30:19

20 Q. Correct. 13:30:21

21 A. And -- you know, the inflammation, by that 13:30:23
22 time, may be reduced because these patients are 13:30:33

1 maximized on their other medications, including 13:30:35
2 statins that have an effect on inflammation. So 13:30:40
3 this additional beneficial effect of colchicine on 13:30:41
4 inflammation during that time may not be as 13:30:43
5 prominent or as significant as you would see it when 13:30:46
6 the inflammation or the inflammatory burden is at 13:30:49
7 the highest point, which would be in the first few 13:30:54
8 days after the myocardial infarction. 13:30:57

9 Q. So in your first declaration in 13:31:25
10 paragraph 48, you discuss statins, and you've 13:31:27
11 referenced statins quite a bit today. 13:31:29

12 Is that -- are statins a drug you're -- you 13:31:34
13 would consider yourself to be an expert on? 13:31:38

14 A. Well, depends on what you -- how you 13:31:42
15 describe an expert on statins. I have given talks 13:31:45
16 on statins. I know how they work. I give it to my 13:31:49
17 patients, and I have been following the studies that 13:31:53
18 have been published on statins. 13:31:56

19 Q. And what are the similarities between 13:31:57
20 statins and colchicine? 13:32:00

21 MR. WILKERSON: Objection to form. 13:32:03

22 A. So what statins do, they inhibit an enzyme 13:32:04

1 called HMG-CoA reductase. And one of the products
2 or the product of this enzyme can also be involved
3 in the production of leukotrienes, and that can have
4 an effect on inflammation.

5 So statins, what they do is they inhibit
6 production of cholesterol from the liver, but they
7 can also have an effect on the inflammatory
8 processes. Colchicine, what it does, it has an
9 effect on microtubules. And microtubules are needed
10 for cell proliferation, cell division. And one of
11 the types of cells in our body that proliferates on
12 a regular basis are the inflammatory cells. So by
13 inhibiting microtubules, they inhibit the
14 proliferation of immune cells.

15 And that's probably why they also have these
16 GI side effects because the epithelial cells in our
17 digestive tract have to regenerate on a regular
18 basis, and that could be the reason why they have
19 these GI side effects.

20 So to answer your question, I would say
21 similarities are that they both can have an effect
22 on the inflammatory processes.

1	Q. Turning back to paragraph 48, you mentioned	13:33:19
2	strengths in the fourth line.	13:33:26
3	Do you see that?	13:33:27
4	A. Yes.	13:33:28
5	Q. Strengths of 40 to 80 milligrams and 20 to	13:33:28
6	40 milligrams. Are you -- do you mean dosage?	13:33:32
7	A. Yes.	13:33:35
8	Q. And what do you mean by strength?	13:33:39
9	A. Dosage.	13:33:41
10	Q. So for a molecule like the statins that are	13:33:48
11	listed, the actual dose is not really indicative	13:34:00
12	of -- excuse me. Strike that.	13:34:10
13	A comparison of milligram quantities is	13:34:12
14	meaningless in the pharmaceutical sense for	13:34:16
15	comparison of statins with colchicine, isn't it?	13:34:19
16	MR. WILKERSON: Objection. Foundation.	13:34:23
17	A. Are you asking the dosage of a statin, would	13:34:28
18	it be comparable to the dosage of colchicine? Is	13:34:32
19	that what you're asking?	13:34:35
20	Q. Yes, just because the volume of the statin	13:34:36
21	is greater than the volume of colchicine isn't	13:34:39
22	indicative of anything, is it?	13:34:44

1	MR. WILKERSON: Objection to form.	13:34:47
2	A. The volume of colchicine is greater than the	13:34:47
3	volume of -- I don't follow that. Sorry.	13:34:50
4	Q. What I'm getting at is, it's not a very	13:34:52
5	accurate way to measure effectiveness?	13:34:56
6	MR. WILKERSON: Same objection.	13:34:59
7	A. Of what?	13:35:01
8	Q. By comparing the volume of the statin that's	13:35:02
9	delivered with the volume of the colchicine, that's	13:35:08
10	not a very informative way of measuring the	13:35:14
11	anti-inflammation effect?	13:35:19
12	MR. WILKERSON: Objection. Form.	13:35:22
13	A. What do you mean by volume? That's what I'm	13:35:23
14	not understanding.	13:35:26
15	Q. So take a minute to read paragraph 48.	13:35:27
16	A. Yes.	13:35:31
17	Okay.	13:36:00
18	Q. So is the objective of paragraph 48, are you	13:36:00
19	trying to compare the impact of statins at those	13:36:07
20	doses with the impact of colchicine at a dosage of	13:36:11
21	0.5 milligrams? Is that what why you're trying to	13:36:16
22	compare?	13:36:19

1	MR. WILKERSON: Objection to form.	13:36:19
2	A. No. So now I understand what you mean by	13:36:20
3	volume. You meant the dosage of these drugs.	13:36:23
4	Q. Yes. Sorry. That was weight, not volume.	13:36:26
5	A. Sure. That's not the point of this	13:36:30
6	paragraph. The point of this paragraph saying -- is	13:36:33
7	that Dr. Ridker was saying that ESC guidelines	13:36:36
8	recommend high-intensity statins to be started	13:36:43
9	early. What I'm saying here is that the	13:36:48
10	anti-inflammatory dosage of -- or anti-inflammatory	13:36:49
11	effects of colchicine, we didn't know at the time	13:36:52
12	that it would lead to similar improvements. So	13:36:55
13	making that comparison that, based on ESC	13:36:59
14	guidelines, everybody would know or a POSA would	13:37:02
15	know that colchicine should be started at an earlier	13:37:06
16	time, this wasn't known. And the study that was	13:37:10
17	done by Dr. B made that clear, that the initiation	13:37:15
18	of colchicine in the time period of 0 do 3 days is	13:37:18
19	very effective in reducing cardiovascular events.	13:37:22
20	Q. Okay. I've got the label for Lipitor. It's	13:37:26
21	Exhibit 1054.	13:37:35
22	///	

1	(Exhibit 1054 was marked for	13:37:35
2	identification and was retained by counsel.)	13:37:53
3	A. Thank you.	13:37:53
4	Q. Are you familiar with this label for	13:38:02
5	Lipitor?	13:38:04
6	A. I think I've seen it before.	13:38:05
7	Q. Do you see on the first page the dosages	13:38:06
8	that are listed?	13:38:11
9	A. Yes.	13:38:12
10	Q. What are the available dosage forms?	13:38:13
11	A. It says dose range 10 to 80 milligram once	13:38:16
12	daily and recommended start dose 10 or 20 milligram	13:38:20
13	once daily.	13:38:23
14	Q. And what is the daily dosage range? Is that	13:38:25
15	what you just read?	13:38:30
16	A. Yeah, 10 to 80.	13:38:31
17	Q. Oh, sorry. Okay.	13:38:33
18	And is this where you got the information	13:38:36
19	for what you included in paragraph 48 about the	13:38:38
20	dosage of 40 to 80 milligrams?	13:38:40
21	A. No.	13:38:42
22	Q. That's just from your personal experience or	13:38:43

1	use or what?	13:38:46
2	A. No. So we have two guidelines in -- two	13:38:46
3	major guidelines in cardiology. One of them is the	13:38:53
4	American Heart Association and American College of	13:38:56
5	Cardiology guidelines. So those are the American	13:38:58
6	guidelines, and the American College of Cardiology	13:39:00
7	and the American Heart Association, they have	13:39:03
8	collaborated to give the same guidelines that come	13:39:06
9	from the U.S. -- you know, the U.S. investigators.	13:39:08
10	And then we have the European guidelines.	13:39:12
11	So that's called ESC guidelines. Of course we have	13:39:14
12	other guidelines. You know, there's a Japanese	13:39:18
13	guidelines, Chinese guidelines. But those are the	13:39:21
14	two major guidelines that are out there.	13:39:24
15	And what I'm referring to in those	13:39:26
16	guidelines -- in that paragraph is the guideline	13:39:29
17	recommendations for the dosage of intensive statin	13:39:31
18	therapy after myocardial infarction. So what we do	13:39:40
19	is that patients who have very high risk factors or	13:39:42
20	if they have had myocardial infarction, we do	13:39:47
21	intensive statin therapy in those patients. And the	13:39:51
22	way that high statin therapy is defined is Lipitor	13:39:55

1 or atorvastatin 40 to 80 milligrams or Crestor or

13:40:01

2 rosuvastatin 20 to 40 milligrams.

13:40:06

3 So the dosages I'm referring to here are for

13:40:10

4 aggressive treatment in patients who are at high

13:40:14

5 risk or patients who have had a myocardial

13:40:17

6 infarction, based on ESC guidelines and American

13:40:20

7 College of Cardiology and American Heart Association

13:40:22

8 guidelines.

13:40:24

9 Q. Okay. And what is Lipitor indicated for?

13:40:25

10 A. So the indications in the label are to

13:40:37

11 Reduce the risk of MI, stroke, revascularization

13:40:41

12 procedures, and angina in adult patients without CHD

13:40:46

13 which is coronary heart disease, but with multiple

13:40:48

14 risk factors.

13:40:51

15 Reduce the risk of MI and stroke in adult

13:40:52

16 patients with type 2 diabetes without CHD but with

13:40:55

17 multiple risk factors.

13:40:58

18 Reduce the risk of nonfatal MI, fatal and

13:41:00

19 nonfatal stroke, revascularization procedures,

13:41:05

20 hospitalization for CHF, and angina in adults

13:41:07

21 patients with CHD.

13:41:11

22 Reduce elevated total cholesterol, LDL

13:41:12

1 cholesterol, apoB, and triglyceride levels and 13:41:16
2 increase HDL cholesterol in adults patients with 13:41:18
3 primary hyperlipidemia (heterozygous familial and 13:41:22
4 nonfamilial) and mixed dyslipidemia. 13:41:30

5 Reduce elevated triglyceride in adult 13:41:30
6 patients with hypertriglyceridemia and primary 13:41:34
7 dysbetalipoproteinemia. 13:41:40

8 Reduce total cholesterol and LDL cholesterol 13:41:42
9 in patients with homozygous familial and 13:41:45
10 hypercholesterolemia. 13:41:50

11 And reduce elevated total cholesterol, LDL 13:41:50
12 cholesterol, and apoB levels in pediatric patients, 13:41:54
13 ten years to 17 years of age, with heterozygous 13:42:03
14 familial hypercholesterolemia after failing an 13:42:07
15 adequate trial of diet therapy. 13:42:10

16 Q. Thank you. In your own words, what is 13:42:12
17 Lipitor contraindicated for? 13:42:14

18 A. Okay. Not reading from here? 13:42:17

19 Q. Correct. 13:42:18

20 A. So patients who have absolute 13:42:20
21 contraindication, which is usually hypersensitivity 13:42:23
22 to the drug, that's the common absolute 13:42:28

1 contraindication. There are patients who get an
2 increase in their liver enzymes, usually we say,
3 when the liver enzymes get above three times upper
4 limit of normal.

5 And patients who have muscle damage, that's
6 called rhabdomyolysis. And patients who get
7 rhabdomyolysis because of statin therapy, that's an
8 absolute contraindication. But sometimes patients
9 get muscle pain. And we stop giving to those
10 patients.

11 Fortunately, I haven't had any of those side
12 effects when I took statins, so that's worked well
13 for me.

14 Q. Love it when a doctor takes a medication he
15 prescribes. That's encouraging.

16 So I have the label for Crestor. And maybe
17 instead of reading the indications, if you could
18 just say either the same as, in general, as Lipitor
19 or just describe it in your own words.

20 A. Yeah, in terms for Crestor --

21 Q. Sorry. Exhibit 1055.

22 ///

1	(Exhibit 1055 was marked for	13:43:45
2	identification and was retained by counsel.)	13:43:49
3	A. Yes, for Crestor, the indications are very	13:43:49
4	similar. But if I am not mistaken --	13:43:51
5	THE VIDEOGRAPHER: Doctor, I can't hear you.	13:43:54
6	Can you uncover your mic? Thank you.	13:43:57
7	A. Crestor has similar indications, but if I'm	13:44:00
8	not mistaken, Crestor has an additional indication	13:44:03
9	that is the only statin that has been indicated by	13:44:06
10	the FDA for a reduction in atherosclerotic plaque	13:44:08
11	volume. So let me just make sure, but I believe	13:44:13
12	that's the only statin that has been indicated for	13:44:16
13	that.	13:44:20
14	Yeah. So that basically in the third bullet	13:44:34
15	point, it says slow deprivation of atherosclerosis	13:44:36
16	in adults. I believe that's the only statin with	13:44:43
17	that indication. And that was based on a clinical	13:44:46
18	study where they did the IVUS, which is	13:44:49
19	intravascular ultrasound, and they showed that	13:44:51
20	statins can reduce atherosclerotic plaque in	13:44:55
21	coronary vessels.	13:44:59
22	Q. What is the source of the daily dosage	13:45:00

1	ranges that you have in your paragraph 38? Is it	13:45:03
2	the same as what you described for Lipitor?	13:45:05
3	A. No, it's 20 to 40 milligrams.	13:45:07
4	Q. No, I mean the source of that.	13:45:11
5	A. Right. So that's from the guidelines, yes.	13:45:12
6	Q. And if you could compare the	13:45:17
7	contraindications for Lipitor and Crestor, what do	13:45:21
8	they have in common?	13:45:24
9	A. In my own words?	13:45:26
10	Q. Yes.	13:45:27
11	A. Yeah, so --	13:45:28
12	Q. Go ahead and take a minute to look at them.	13:45:33
13	A. Right. So for Crestor, it says	13:45:35
14	hypersensitivity to rosuvastatin or any excipient in	13:45:38
15	Crestor or acute liver failure or decompensated	13:45:46
16	cirrhosis. So those are the contraindications.	13:45:50
17	And then for Lipitor, are acute liver	13:45:53
18	disease, which may include unexplained persistent	13:45:55
19	elevations in hepatic transaminase levels,	13:45:59
20	hypersensitivity to any components of this	13:46:02
21	medication, pregnancy, and lactation.	13:46:05
22	Q. So what's the main ones that they have in	13:46:06

1	common?	13:46:12
2	MR. WILKERSON: Objection to form.	13:46:13
3	A. So it would be hypersensitivity to the drugs	13:46:13
4	or any components of the drugs and also acute liver	13:46:17
5	failure or hepatic impairment.	13:46:20
6	Q. Okay. I'm handing you Exhibit 1057.	13:46:30
7	(Exhibit 1057 was marked for	13:46:30
8	identification and was retained by counsel.)	13:46:40
9	Q. This is the label for LoDoCo. Are you	13:46:40
10	familiar with this document?	13:46:43
11	A. I don't think I've seen this before.	13:46:48
12	Q. So do you see that the label for LoDoCo, or	13:47:05
13	colchicine, indicates that the recommended dosage is	13:47:11
14	0.5 milligrams orally once daily?	13:47:16
15	A. Yes.	13:47:20
16	Q. Do you see any time periods that are	13:47:20
17	recommended for beginning treatment with colchicine?	13:47:28
18	MR. WILKERSON: Objection. Form.	13:47:48
19	A. So not directly, but there are some	13:49:12
20	information regarding the half-life or T-half hours	13:49:15
21	in table 2 under "Pharmacokinetics." So that talks	13:49:23
22	about how long it takes for the drug to be	13:49:27

1 eliminated. And then it talks about T-max hours 13:49:31
2 also, how long it takes for the drug to have the -- 13:49:34
3 you know, to get to the maximal therapeutic range. 13:49:38

4 And then there's some -- there's some 13:49:44
5 information on the page 13 under "Clinical Studies" 13:49:48
6 that refers to LoDoCo 2 study. And it also talks 13:49:52
7 about patients who were clinically stable for at 13:49:56
8 least six months. 13:50:06

9 So those are the only time points that I 13:50:10
10 could find in this protocol. 13:50:14

11 Q. And what are the indications that are listed 13:50:16
12 on the first page? 13:50:19

13 A. So it says, [As read] To reduce the risk of 13:50:21
14 myocardial infarction, stroke, coronary 13:50:25
15 revascularization and, cardiovascular death in adult 13:50:27
16 patients with established atherosclerosis disease or 13:50:33
17 with multiple risk factors for cardiovascular 13:50:35
18 disease. 13:50:38

19 Q. And does that overlap with the indications 13:50:38
20 for the statins? 13:50:40

21 MR. WILKERSON: Objection to form. 13:50:42

22 A. Some of it does, yes. 13:50:52

1	Q. And what is LoDoCo contraindicated for?	13:50:57
2	A. So the contraindications are, "Concurrent	13:51:02
3	use of strong CYP3YA4 inhibitors" -- that's a	13:51:08
4	cytochrome P-450, isoform 3A4 -- "or P-gp" --	13:51:13
5	that's -- I think that's phospho- -- glycoprotein --	13:51:18
6	"inhibitors with LoDoCo is contraindicated,	13:51:25
7	including in patients with hepatic or renal	13:51:28
8	impairment."	13:51:30
9	And then it also says that [As read] LoDoCo	13:51:31
10	is contraindicated in patients with preexisting	13:51:33
11	blood dyscrasias, renal failure, and severe hepatic	13:51:36
12	impairment.	13:51:42
13	Q. Is there overlap in the contraindications?	13:51:46
14	A. Yes.	13:51:49
15	Q. And how did the FDA treat colchicine --	13:51:49
16	excuse me. Strike that.	13:51:56
17	Did the FDA treat colchicine the same as it	13:51:57
18	treats statins?	13:52:01
19	MR. WILKERSON: Objection to form.	13:52:02
20	A. What do you mean if the FDA treats these two	13:52:03
21	drugs differently?	13:52:08
22	Q. Strike the question.	13:52:09

1	So do you agree that the FDA has approved	13:52:10
2	colchicine for cardiovascular disease treatment?	13:52:19
3	A. In this protocol, it appears to, yes.	13:52:25
4	Q. This is -- you agree this is a label, not a	13:52:28
5	protocol?	13:52:34
6	A. I'm sorry. Yes. In this label, yes.	13:52:35
7	Q. Based on this label, would you be	13:52:37
8	comfortable prescribing colchicine at any time after	13:52:48
9	a patient becomes stable?	13:52:55
10	MR. WILKERSON: Objection to form.	13:52:58
11	A. Well, I don't just use one source for my	13:52:59
12	practice. I don't just look at the drug label. In	13:53:03
13	fact, the majority of the drugs I give to my	13:53:06
14	patients, I haven't even looked at the label. It's	13:53:10
15	our clinical judgment and what's in our clinical	13:53:13
16	knowledge that plays a role in our -- in prescribing	13:53:18
17	a medication.	13:53:21
18	So I would say no. I have more information	13:53:22
19	and the information I have is that patients, after	13:53:27
20	their myocardial infarction and if they undergo	13:53:31
21	angioplasty, in those patients, I would be very	13:53:34
22	aggressive and give them this medication within	13:53:37

1 3 days. And in patients who have coronary artery
2 disease and have multiple risk factors for
3 cardiovascular disease, I would consider, definitely
4 consider colchicine in those patients.

5 Q. So would you consider the Bouabdallaoui
6 reference, which is a post hoc analysis, to take
7 precedence over clinical trials like LoDoCo 1 and 2,
8 COLCOT, and the FDA label?

9 MR. WILKERSON: Objection to form.

10 A. No. I wouldn't give one more priority than
11 others. I would say that I would take everything
12 into consideration like every other practicing
13 cardiologist in this country.

14 Q. Do you agree that in addition to Nidorf, the
15 patent that we looked at, the COLCOT study also is
16 silent about a loading dose?

17 A. The COLCOT study itself? The study itself
18 is .5-milligram colchicine per day. It doesn't talk
19 about specifically excluding it, no.

20 Q. In your first declaration -- excuse me.

21 In your first declaration on page 23 and
22 bridging over to 24 in paragraph 50, you state

1 that -- you make a reference to a motivation for a 13:55:54
2 person of ordinary skill in the art to combine 13:56:03
3 references. 13:56:05

4 Can you explain what you mean by motivation 13:56:06
5 to combine references? 13:56:15

6 MR. WILKERSON: Objection. Form. 13:56:20

7 A. So there are a couple of different reasons. 13:56:43
8 So if you look at these studies, first of all, 13:56:50
9 COLCOT, Nidorf, and ESC guidelines, they are 13:56:54
10 different studies. So ESC guidelines don't talk 13:57:00
11 about colchicine. COLCOT was, you know, looking at 13:57:03
12 cardiovascular events with colchicine, and stroke 13:57:13
13 was just one of the factors that was included in 13:57:18
14 there. And Nidorf is, basically, LoDoCo study where 13:57:22
15 they looked at colchicine in patients who were 13:57:32
16 stabilized after six months since their myocardial 13:57:34
17 infarction. 13:57:38

18 So what I'm saying is that those studies are 13:57:39
19 separate studies looking at different things or in 13:57:43
20 terms of, you know, studies and guidelines, there 13:57:46
21 are different things. And so there would be no 13:57:49
22 reason to combine them to come up with -- to come up 13:57:52

1 with any reason -- to come up with this conclusion 13:57:56
2 that colchicine would reduce risk of stroke, as 13:58:01
3 recited in Claim 27. 13:58:04

4 The other point I'm making here is that 13:58:07
5 there was contradictory data in terms of the effects 13:58:10
6 of colchicine on cardiovascular events, including 13:58:13
7 stroke. And there was no reasonable expectation 13:58:19
8 that this would be positive. There were several 13:58:23
9 studies in the past that had shown that colchicine 13:58:26
10 may not reduce CRP. It may not be effective in 13:58:28
11 reducing cardiovascular events, and so there was no 13:58:33
12 clear expectation that, you know, this medication 13:58:36
13 would be beneficial until COLCOT was done. 13:58:42

14 Q. Would you agree that knowing that a 13:58:44
15 medication has a therapeutic benefit, would a person 13:58:46
16 of ordinary skill in the art be motivated to start 13:58:50
17 treatment with the medication sooner or later? 13:58:51

18 MR. WILKERSON: Objection. Legal 13:58:53
19 conclusion. 13:58:55

20 A. That would really depend on what kind of 13:58:56
21 data you have. If the data is convincing, you would 13:58:59
22 try to use it as soon as possible. If the data is 13:59:04

1 not convincing, you would wait for additional data 13:59:07
2 to come out. 13:59:11

3 Q. Do you agree that patients that start a 13:59:11
4 treatment in the hospital are more likely to 13:59:13
5 continue taking the treatment than those that start 13:59:16
6 a treatment after discharge? 13:59:18

7 MR. WILKERSON: Objection to form. 13:59:24

8 A. It really depends on what it is indicated 13:59:29
9 for. I -- most of my patients, if I tell them that 13:59:32
10 they should take a medication, even when they're in 13:59:37
11 clinic, I send it to their pharmacy. You know, 13:59:41
12 these days it just -- the medication goes directly 13:59:45
13 to the pharmacy and they get it and they take it. 13:59:47
14 So I don't think I would agree with that statement. 13:59:50
15 In general, it's probably correct but it's hard for 13:59:57
16 me to tell one way or the other, based on my 14:00:00
17 experience in my practice. 14:00:03

18 Q. Well, for example, with statins, those 14:00:04
19 are -- are those typically prescribed in the 14:00:08
20 hospital -- 14:00:10

21 A. Really -- 14:00:12

22 Q. -- after an MI or a stroke? 14:00:12

1 A. Right. Sure. For those, yes. For those 14:00:14
2 you have to start it in the hospital, unless there 14:00:17
3 is a clear contraindication. 14:00:20

4 Q. And what's the reason for doing so? 14:00:21

5 A. So what you want to do, you basically -- in 14:00:23
6 the setting of an MI, you know that you have to -- 14:00:26
7 first of all, these patients, there is a clear 14:00:30
8 indication for this medication. And what we do is 14:00:32
9 that we do guideline-directed medical therapy. We 14:00:36
10 call it GDMT. Guideline-directed medical therapy. 14:00:39
11 And our practice is based on guidelines. So if 14:00:44
12 there is something that is indicated in the 14:00:47
13 guidelines, we start it in the hospital, and we try 14:00:48
14 to make sure that the patient is given all of these 14:00:51
15 medications. But we know that in the setting of 14:00:53
16 myocardial infarction, statins are probably helpful 14:00:56
17 because they stabilize the plaque. So there are 14:01:00
18 multiple -- several reasons why they are started on 14:01:03
19 statins in the hospital. 14:01:06

20 Q. In your second declaration at paragraph 12, 14:01:07
21 you refer to O'Keefe study. And I'm handing you a 14:01:42
22 copy of Exhibit 2009, which is the O'Keefe study. 14:01:49

1	(Exhibit 2009 was marked for	14:01:49
2	identification and was retained by counsel.)	14:01:58
3	A. You couldn't make the text any smaller?	14:01:58
4	Q. With that small font, can you see what year	14:02:06
5	it was published?	14:02:09
6	A. 1992.	14:02:09
7	Q. Okay. And in paragraph 12 of your first	14:02:12
8	declaration, you talk about O'Keefe.	14:02:19
9	Do you see that?	14:02:23
10	Second declaration. Sorry.	14:02:40
11	A. Yes.	14:02:55
12	Q. And you state that [As read] O'Keefe found	14:02:56
13	that colchicine was not effective compared to	14:03:03
14	placebo at preventing cardiovascular disease in the	14:03:06
15	studied population.	14:03:11
16	A. Right.	14:03:12
17	Q. Do you know what the focus of O'Keefe was?	14:03:13
18	A. Yeah. If I'm not mistaken, they were	14:03:17
19	looking at the degree of blockage in coronary	14:03:20
20	vessels.	14:03:23
21	Q. And what end points was O'Keefe trying to	14:03:23
22	test?	14:03:26

1	A. So they were using angiography to assess the	14:03:56
2	degree of blockage in coronary vessels, and they	14:04:02
3	were doing it at time 0 and at, I believe, 6 months	14:04:05
4	after angioplasty.	14:04:13
5	Q. And what was the treatment regimen?	14:04:15
6	A. Colchicine 0.6-milligram daily or placebo.	14:04:21
7	Q. Twice daily?	14:04:27
8	A. I'm sorry. Twice daily. Sorry. This is --	14:04:29
9	the font is too small.	14:04:33
10	Q. And does O'Keefe use a loading dose?	14:04:34
11	A. No.	14:05:19
12	Q. And do you consider O'Keefe to be indicative	14:05:21
13	of the state of the art at the time of the priority	14:05:27
14	date of the '063 patent? So the relevant time	14:05:32
15	period?	14:05:37
16	MR. WILKERSON: Objection to form.	14:05:38
17	A. I believe so. I mean, again, in 1992, I was	14:05:39
18	a second-year medical student, so that was a long	14:05:42
19	time ago and at that time, doing angiography to look	14:05:45
20	at coronary blockage. That was the state of the art	14:05:50
21	at the time.	14:05:54
22	Q. But not at the time period of 2019?	14:05:55

1	A. What do you mean --	14:06:15
2	MR. WILKERSON: Objection to form.	14:06:16
3	A. -- the "time period"?	14:06:17
4	Q. So O'Keefe was relevant in 1992; right?	14:06:20
5	A. Well, it's a scientific paper, and it's	14:06:24
6	relevant all the time.	14:06:28
7	Q. But have there been other publications since	14:06:29
8	1992 and before 2019 that are perhaps more	14:06:31
9	indicative of the state of the art in 2019?	14:06:38
10	MR. WILKERSON: Objection to form.	14:06:42
11	A. Depends on what question they looked at.	14:06:44
12	But, you know, sometimes we go back to papers from	14:06:48
13	decades ago, and they are still relevant.	14:06:53
14	Q. But this is under the topic of what is	14:06:56
15	predictable. And are there papers that came since	14:06:59
16	1992 that indicate that colchicine -- that outcomes	14:07:04
17	for patients using colchicine, that that's	14:07:10
18	predictable?	14:07:14
19	MR. WILKERSON: Objection to form.	14:07:15
20	A. Yes, and that's the point I'm making. There	14:07:16
21	are studies that have shown beneficial effects, and	14:07:19
22	there are studies that have not shown beneficial	14:07:22

1	effects, so there are contradictory data in the	14:07:25
2	literature.	14:07:27
3	Q. But isn't it more instructive to look at	14:07:28
4	more recent publications?	14:07:31
5	MR. WILKERSON: Objection to form.	14:07:35
6	A. I would say it's instructive to look at	14:07:37
7	everything that is in the literature. And I don't	14:07:39
8	think there are any other studies where they use	14:07:43
9	angiography to look at coronary blockage and to look	14:07:45
10	at the effects of colchicine on coronary blockage.	14:07:49
11	This is the only study that I can think of that has	14:07:52
12	been published and that is in the literature that	14:07:56
13	looks at that specific question.	14:07:58
14	MR. LAURENCE: We can take a break.	14:08:29
15	THE WITNESS: Okay. Thank you.	14:08:32
16	THE VIDEOGRAPHER: Going off the record at	14:08:33
17	2:07 p.m.	14:08:35
18	(A short break was had.)	14:08:36
19	THE VIDEOGRAPHER: Going back on the record	14:21:13
20	at 2:20 p.m.	14:21:27
21	BY MR. LAURENCE:	14:21:29
22	Q. I'm handing you a copy of Exhibit 2054.	14:21:31

1	(Exhibit 2054 was marked for	14:21:31
2	identification and was retained by counsel.)	14:21:37
3	Q. Are you familiar with this document?	14:21:37
4	A. Yes.	14:21:39
5	Q. And what did Raju teach?	14:21:44
6	MR. WILKERSON: Objection. Form.	14:21:51
7	A. So this paper looks at the effects of	14:21:55
8	colchicine versus placebo on high sensitivities to	14:21:59
9	reactive proteins in patients with acute coronary	14:22:06
10	syndrome or acute stroke, and it was a pilot	14:22:10
11	randomized control trial. And it basically showed	14:22:14
12	that there was no evidence that colchicine	14:22:17
13	1 milligram daily for 30 days, compared to placebo,	14:22:20
14	suppresses inflammation in patients with acute	14:22:25
15	coronary syndrome or acute ischemic stroke.	14:22:27
16	Q. And did Raju just look at CRP levels at	14:22:31
17	baseline and then at 30 days?	14:22:36
18	A. They looked at the CRP levels and platelet	14:22:47
19	functions at two time points, day 0 and day 80 --	14:22:55
20	I'm sorry -- day 30.	14:22:59
21	Q. And did Raju look at any clinical outcomes?	14:23:01
22	A. No.	14:23:09

1	MR. WILKERSON: Objection to form.	14:23:09
2	Q. Is it fair to say that Raju looked at a	14:23:10
3	biomarker but not long-term chronic clinical end	14:23:13
4	points?	14:23:17
5	MR. WILKERSON: Objection to form.	14:23:17
6	A. Yes.	14:23:18
7	Q. I'm handing you a copy of Exhibit 1028.	14:23:18
8	(Exhibit 1028 was marked for	14:23:18
9	identification and was retained by counsel.)	14:23:29
10	Q. To Hennessy.	14:23:29
11	Are you familiar with this document?	14:23:38
12	A. Yes.	14:23:40
13	Q. What did Hennessy teach?	14:23:41
14	A. So in this paper, they looked at low-dose	14:23:44
15	colchicine, which was .5 milligram daily, and they	14:23:55
16	randomized patients to either colchicine or placebo,	14:24:00
17	and there were 237 patients admitted with acute	14:24:07
18	myocardial infarction. They looked at proportion of	14:24:12
19	patients with residual high-sensitivity CRP levels	14:24:18
20	of greater than 2 milligrams per liter after 30 days	14:24:24
21	of treatment.	14:24:27
22	Q. And what were the end points?	14:24:30

1 A. Right. So what they saw was that the
2 treatment with this regimen of colchicine was safe
3 and well tolerated but was not associated with a
4 significantly increased likelihood of achieving a
5 CRP level less than 2 milligram per liter or lower
6 absolute level of CRP 30 days after an acute MI.

7 Q. And what was the duration of the study?

8 A. So it was 30 days of treatment.

9 Q. And it looked at CRP levels, not clinical
10 end points; correct?

11 MR. WILKERSON: Objection. Form.

12 A. Right. So they are looking at the biomarker
13 that correlates with worst prognosis.

14 Q. And does Hennessy teach that colchicine is
15 safe to use close to acute MI?

16 A. Well, they showed that, in patients with
17 acute MI -- and, again, these are not patients
18 who -- patient who were -- who underwent a coronary
19 angioplasty. Within a 30-day period, this treatment
20 was safe during that 30-day period.

21 Q. Okay. And that was after acute MI? I'm
22 looking at page 69, first column, first paragraph

1	that says "In conclusion."	14:26:11
2	A. So yes, so it says, [As read] In conclusion,	14:26:18
3	we found no significant reduction in the median	14:26:21
4	level of CRP, the absolute or relative reduction in	14:26:24
5	the levels, or the percentage of patients who had	14:26:28
6	levels of CRP below 2 milligram per liter after	14:26:31
7	30 days. All were --	14:26:35
8	Q. I'm skipping down to the very last few words	14:26:36
9	of that paragraph.	14:26:40
10	A. Yeah, so it basically says, [As read]	14:26:42
11	Importantly, in this regard, the current study	14:26:45
12	demonstrates the safety and tolerability of low-dose	14:26:48
13	colchicine after acute MI.	14:26:51
14	But this was just looking at 30 days --	14:26:53
15	Q. Okay.	14:26:56
16	A. -- which is a very short time period.	14:26:56
17	That's not what you usually -- we usually consider	14:26:59
18	to be -- to make a conclusion about the safety of a	14:27:02
19	drug.	14:27:06
20	Q. But isn't that the same time period from	14:27:06
21	Raju, 30 days?	14:27:09
22	A. Correct. So this was after -- after acute	14:27:20

1 coronary syndrome or acute ischemic stroke. 14:27:23

2 Q. Okay. 14:27:27

3 A. But that one was after acute myocardial 14:27:28
4 infarction. 14:27:33

5 Q. And I'm handing you Exhibit 2055. 14:27:33

6 (Exhibit 2055 was marked for 14:27:33
7 identification and was retained by counsel.) 14:27:45

8 A. Thank you. 14:27:45

9 Q. And this is the Akodad references. Are you 14:27:45
10 familiar with this document? 14:27:59

11 A. Yes. 14:27:59

12 Q. What did Akodad -- did I pronounce it 14:28:00
13 correctly? 14:28:04

14 A. I think so. 14:28:05

15 Q. What did Akodad teach? 14:28:05

16 A. So the aim of this study was to evaluate the 14:28:14
17 impacts of the colchicine on inflammation in 14:28:17
18 patients admitted for ST-segment elevation 14:28:20
19 myocardial infarction. And 44 patients were 14:28:24
20 included. 14:28:25

21 Q. Is that a pretty small number? 14:28:25

22 A. Yes. Well, that's a relatively small 14:28:27

1 number.

14:28:31

2 23 were treated with colchicine. 20 were --
3 received conventional treatment only. And patients
4 were given 1 milligram of colchicine once daily for
5 one month plus optimal medical treatment or optimal
6 medical treatment only, and C-reactive protein was
7 assessed at admission and daily until hospital
8 discharge. The primary end point was CRP peak value
9 during the index hospitalization.

14:28:32

14:28:34

14:28:49

14:28:53

14:28:56

14:29:02

14:29:06

14:29:09

10 What they saw was that the effect of
11 colchicine on the inflammation in the context of
12 ischemia could not be demonstrated, and that was
13 what the conclusion was.

14:29:12

14:29:13

14:29:18

14:29:21

14 Q. So what were some of the limitations of this
15 study?

14:29:22

14:29:24

16 MR. WILKERSON: Objection to form.

14:29:30

17 A. So there is a section on study limitations,
18 and that's what the authors felt that it was their
19 study limitations. It says, [As read] Many study
20 limitations have to be discussed, despite the
21 prospective, randomized design: The small number of
22 patients included in a single-center study; the low

14:29:38

14:29:40

14:29:44

14:29:49

14:29:54

14:29:58

1	statistical power; and the imbalanced population,	14:30:01
2	especially regarding clinical characteristics. The	14:30:04
3	STEMI population was particularly heterogeneous,	14:30:07
4	with a different infarct size according to the	14:30:10
5	culprit artery. In the colchicine group, the LAD	14:30:13
6	was involved in the majority of the cases, whereas	14:30:16
7	in the control group, the RCA was more often	14:30:18
8	involved. However, we showed that the CRP peak	14:30:23
9	value were not significantly different, even after	14:30:27
10	adjusting for the culprit artery, suggesting that	14:30:29
11	the lack of effect may not be the result of a more	14:30:33
12	important infarct size in the colchicine group.	14:30:36
13	Moreover, the study population presented a small	14:30:40
14	level of inflammation, in comparison with the	14:30:43
15	population that is classically encountered in this	14:30:46
16	context, with values of CRP peak less than 30	14:30:49
17	milligram per liter in the two study groups, whereas	14:30:53
18	we expected a peak of about 60 milligrams per liter.	14:30:56
19	Thus, our population was probably not an appropriate	14:31:01
20	target population to benefit from an	14:31:04
21	anti-inflammatory therapy to answer this study	14:31:06
22	hypothesis. Another limitation of the study was the	14:31:09

1 lack of placebo in the control group, and therefore
2 the open-label design. However, as the primary end
3 point of this preliminary study was an objective
4 biological criterion, we believe that the impact of
5 such a design on the results may have been very low.
6 Nevertheless, our results should be replicated in a
7 study evaluated clinical -- I'm sorry -- evaluating
8 clinical end points with a placebo-controlled
9 double-blind design.

10 Q. Okay. And how long were the patients
11 followed?

12 A. It was one month.

13 Q. So would you agree that the short follow-up
14 period suggests that they were -- what they were
15 looking at is the effect of administering colchicine
16 shortly after the acute phase?

17 MR. WILKERSON: Objection to form.

18 A. Sorry. Can you repeat that?

19 Q. Isn't it true that the short 30 days
20 follow-up suggests that what they were looking at is
21 the effect of administering colchicine shortly after
22 the acute phase?

1	MR. WILKERSON: Objection. Form.	14:32:40
2	Q. In other words, is this not a study into the	14:32:46
3	effect on chronic disease?	14:32:49
4	MR. WILKERSON: Objection. Form.	14:32:50
5	A. Yeah, they are looking at the effects of the	14:32:51
6	drug on inflammation at 30 days after treatment with	14:32:54
7	colchicine. So they are trying to see in these	14:32:59
8	patients who have significant myocardial infarction.	14:33:03
9	So STEMI is a significant myocardial infarction.	14:33:07
10	They are trying to see if they can reduce	14:33:13
11	inflammatory markers within 30 days if they started	14:33:15
12	right after myocardial infarction. And they saw	14:33:19
13	that there was no reduction in inflammatory markers.	14:33:22
14	Q. So isn't it true that, if taken at face	14:33:27
15	value, despite the study limitations that you read,	14:33:30
16	that this study, possibly in combination with Raju	14:33:33
17	and Hennessy, shows that colchicine has no effect on	14:33:36
18	short-term end points when initiated on the first	14:33:40
19	day of the AMI or possibly the first two or three	14:33:43
20	days?	14:33:50
21	MR. WILKERSON: Objection. Form.	14:33:50
22	A. Well, what it shows is that, if you are	14:33:52

1 looking at inflammatory markers, the inflammatory
2 markers are not significantly reduced, if
3 colchicine's started within 30 days, or started
4 early after myocardial infarction and, after
5 30 days, there's no significant reduction in
6 C-reactive protein, which is a marker of
7 inflammation. That's all it says.

8 Q. So I'm handing you 2056, Exhibit 2056.

9 (Exhibit 2056 was marked for
10 identification and was retained by counsel.)

11 Q. Are you familiar with this document?

12 A. Yes.

13 Q. What is it?

14 A. It's the COPS clinical trial.

15 Q. And what is the study about?

16 A. So the study was designed to look at the
17 potential effects of colchicine treatment in
18 patients with acute coronary syndrome, or ACS. So
19 this was a multicentered randomized double-blind
20 placebo-controlled study of 17 hospitals in
21 Australia. They had 80 patients who were admitted
22 to acute cardiac care service. And they had acute

1	coronary syndrome. And --	14:35:33
2	Q. Did --	14:35:37
3	A. Sorry.	14:35:39
4	Q. Go ahead.	14:35:41
5	A. And they had evidence of coronary artery	14:35:42
6	disease on coronary angiography. They were treated	14:35:45
7	either with PCI or medical therapy. They were	14:35:48
8	assigned to receive colchicine .5 milligram twice	14:35:51
9	daily for the first month and then .5 milligrams for	14:35:55
10	11 months or placebo. And they were followed up for	14:35:58
11	a minimum of 12 months. And the primary end point	14:36:04
12	was composite of all-cause mortality, ACS,	14:36:09
13	ischemia-driven urgent revascularization, and	14:36:14
14	noncardioembolic ischemic stroke in a time to event	14:36:14
15	analysis.	14:36:20
16	Q. Did they perform a post hoc analysis to look	14:36:20
17	at cardiovascular death as an end point rather than	14:36:24
18	total death?	14:36:27
19	A. Well, they looked at cardiovascular death	14:36:54
20	versus death from any cause, and they included the	14:36:56
21	data in table 2. And in table 2, they saw that	14:36:59
22	cardiovascular death there were three in the	14:37:05

1 colchicine group and one in the placebo group, and 14:37:07
2 that didn't reach a statistical significance. But 14:37:10
3 death from any cause, there were eight in the 14:37:14
4 colchicine group and one in the placebo group, and 14:37:16
5 that reached a statistical significance. 14:37:19

6 Q. And does Tong say that colchicine had an 14:37:32
7 effect on the original, primary outcomes composite 14:37:37
8 at 400 days? 14:37:42

9 A. No. This one is not associated with a 14:37:43
10 reduction in the primary end point. 14:37:47

11 Q. What's your understanding of the row 14:37:56
12 under -- at 400 days in that table 2, primary 14:38:00
13 composite end point and the P value of 0.053? 14:38:04

14 And then the composite end point in this 14:38:16
15 column right here is stated at 400 days. 14:38:18

16 MR. WILKERSON: Objection to form. 14:38:29

17 Q. So the question was, doesn't this say that 14:38:32
18 colchicine did have an effect on the original 14:38:35
19 primary outcome's composite at 400 days? 14:38:38

20 MR. WILKERSON: Objection to form. 14:38:43

21 Q. Maybe read the paragraph ending on that same 14:38:45
22 page where it says at 400 days. 14:38:49

1 A. Right. So again, that was a post hoc 14:40:08
2 analysis. And in this post hoc analysis, they 14:40:10
3 didn't include the -- they only used the 14:40:15
4 cardiovascular death rather than total death. And 14:40:24
5 they saw a significant reduction in the primary 14:40:27
6 outcome between groups in favor of colchicine. 14:40:30

7 Q. Do you trust this post hoc analysis or agree 14:40:48
8 with it? 14:40:56

9 A. Well, it's one piece of the puzzle here. 14:40:56
10 Basically, they're -- you know, this paper came out 14:40:59
11 around the same time as Dr. B's paper. And it 14:41:04
12 basically adds to the confusion, you know, whether 14:41:09
13 or not there is -- you know, there is benefit with 14:41:13
14 colchicine patients with acute coronary syndrome. 14:41:17
15 So, you know, there are contradictory data in the 14:41:20
16 literature. 14:41:23

17 Q. But why trust one and not the other? 14:41:24

18 What's your basis? 14:41:29

19 MR. WILKERSON: Objection to form. 14:41:30

20 A. What do you mean? 14:41:32

21 Q. Well, you embraced the post hoc analysis in 14:41:33
22 Dr. Bouabdallaoui's paper, but do you also agree and 14:41:39

1 accept the post hoc analysis of the COP study? 14:41:47

2 A. Yeah. As I said earlier, yes, I'm taking 14:41:53
3 that into consideration for -- in my analysis. But 14:41:56
4 the thing is that here, we have only 80 patients. 14:41:59
5 So -- but in COLCOT, we had a very large number of 14:42:06
6 patients, and there was enough to do a subgroup 14:42:11
7 analysis and looking at the treatment period for 14:42:15
8 those patients. So there was more information with 14:42:18
9 this post hoc analysis with COLCOT and what Dr. B 14:42:22
10 did. 14:42:27

11 And this is a smaller study, and the level 14:42:28
12 of confidence in this post hoc analysis is probably 14:42:31
13 lower than the level of confidence any physician or 14:42:34
14 any scientist would have in the other study. 14:42:38

15 Q. And what's your rationale for stating in 14:42:41
16 your second declaration in paragraph 17 that Tong 14:42:56
17 shows low-dose colchicine was not effective to treat 14:43:08
18 certain cardiovascular events when compared to 14:43:12
19 placebo? 14:43:16

20 A. You said paragraph 17? 14:43:28

21 Q. Correct. 14:43:29

22 A. Well, that was the conclusion of the paper. 14:43:44

1 If you look at their abstract, that's what their
2 conclusion was.

3 Q. And what's your basis for agreeing with
4 them?

5 A. I -- I agree with their conclusion. I mean,
6 I'm repeating what their conclusion of the paper
7 was. I'm not saying that my practice is gonna be
8 based on their -- on this paper and the results of
9 this paper. I'm just saying the conclusion of the
10 paper was that colchicine is not effective in
11 reducing cardiovascular events.

12 Q. Okay. And do you agree or disagree with the
13 statement on page 6 of the PDF, page 1895, at the
14 bottom of the first column, where it concludes
15 [As read] There was a nominally significant
16 reduction in events using cardiovascular death in
17 the post hoc analysis of the composite end point at
18 400 days.

19 MR. WILKERSON: Objection. Asked.

20 A. I agree with that conclusion, yes.

21 Q. I'm handing you a copy of Exhibit 1051.

22 ///

1	(Exhibit 1051 was marked for	14:45:47
2	identification and was retained by counsel.)	14:45:54
3	Q. Are you familiar with this document?	14:45:54
4	A. I don't think so.	14:45:58
5	Q. Do you know what the acronym CADTH stands	14:46:07
6	for?	14:46:15
7	A. Well, it looks like it stands for Canadian	14:46:15
8	Journal of Health Technologies or no? I'm not sure.	14:46:19
9	Think it's Canadian Healthcare -- no, never mind.	14:46:38
10	Sorry.	14:46:37
11	All right. Now I know. Sorry. It's	14:46:40
12	Canadian Agency for Drugs and Technologies in	14:46:43
13	Health.	14:46:46
14	Q. Okay.	14:46:46
15	A. Finally, I got it.	14:46:47
16	Q. And can you see who this is prepared by and	14:46:49
17	who is the sponsor?	14:46:57
18	MR. WILKERSON: Objection. Form.	14:47:01
19	A. It says the sponsor is Pendopharm, a	14:47:04
20	division of Pharmascience, Incorporation.	14:47:10
21	Q. So is it correct that this is a document	14:47:18
22	prepared by the patent owner?	14:47:21

1	MR. WILKERSON: Objection to form.	14:47:23
2	A. I don't know. I can tell you who the	14:47:27
3	sponsor is, but I don't know who prepared this.	14:47:29
4	Q. Excuse me. Not prepared by, but who	14:47:31
5	sponsored it.	14:47:36
6	MR. WILKERSON: Object to form.	14:47:37
7	Q. Is it fair to say this is sponsored by the	14:47:39
8	patent owner?	14:47:45
9	MR. WILKERSON: Objection to form.	14:47:46
10	A. What patent owner?	14:47:47
11	Q. Pharmascience.	14:47:48
12	A. Which patent are you talking about?	14:47:50
13	Q. The owner of the '063 patent is MHI and	14:47:51
14	Pharmascience.	14:47:58
15	MR. WILKERSON: Objection. Form.	14:47:58
16	Q. And the -- okay. Strike that. I'll	14:48:00
17	rephrase it.	14:48:09
18	Do you know if Pharmascience is the licensee	14:48:10
19	of the patent owned by MHI?	14:48:13
20	A. I think I've heard that before. I don't	14:48:18
21	know the details.	14:48:22
22	Q. Can you see in this document what four	14:48:32

1	trials were considered by the Canadian Drug Expert	14:48:35
2	Committee.	14:49:13
3	Just to expedite --	14:49:13
4	A. Yeah, I found it.	14:49:15
5	Q. -- if you can see the heading "Rationale for	14:49:16
6	the Recommendation" on page 4.	14:49:18
7	Do you see that?	14:49:20
8	A. Yeah. And it says, [As read] Four	14:49:20
9	randomized control trials that enrolled adults with	14:49:22
10	an acute myocardial infarction (COLCOT), stable	14:49:27
11	coronary artery disease (LoDoCo 2, LoDoCo), or acute	14:49:30
12	coronary syndrome (COPS), showed statistically	14:49:32
13	significant differences in the time to first	14:49:37
14	occurrence of an adjudicated major cardiovascular	14:49:38
15	event (a composite end point) favoring colchicine as	14:49:41
16	add-on to standard secondary prevention therapy	14:49:47
17	relative to placebo.	14:49:50
18	Q. So is it accurate to say that the four	14:49:54
19	studies that are relied upon are the COLCOT,	14:49:57
20	LoDoCo 1, LoDoCo 2, and COPS studies?	14:50:00
21	A. Yes.	14:50:03
22	Q. And what is the conclusion that this	14:50:03

1	document comes to?	14:50:07
2	A. So I'm looking at the summary page, and it	14:50:47
3	says CADTH.	14:50:50
4	Q. On what page?	14:50:53
5	A. Summary. That's page 3.	14:50:54
6	Q. Okay.	14:51:00
7	A. So it says, "CADTH recommends that	14:51:01
8	Myinfla" -- I don't know if that's the right	14:51:11
9	pronunciation -- "should not be reimbursed by public	14:51:12
10	drug plans for the reduction of atherothrombotic	14:51:17
11	events in adults with coronary artery disease."	14:51:21
12	Q. Okay. And what is the conclusion on page 7,	14:51:24
13	at the bottom paragraph in the first sentence?	14:51:29
14	A. So it says, [As read] Across all four	14:51:35
15	trials, the time-to-event analyses of the individual	14:51:45
16	components of the primary composite end point showed	14:51:48
17	point estimates for the hazard ratio that favored	14:51:52
18	colchicine versus control. However, the 95 percent	14:51:56
19	confidence interval did not exclude the null for all	14:52:01
20	outcomes.	14:52:06
21	Q. I'm handing you exhibit Exhibit 1053.	14:52:51
22	///	

1	(Exhibit 1053 was marked for	14:52:51
2	identification and was retained by counsel.)	14:53:14
3	Q. Are you familiar with this document?	14:53:14
4	A. No. I don't think I've seen this before.	14:53:16
5	Q. And what is Exhibit 1053 titled?	14:53:47
6	A. It says, "CADTH Reimbursement Review	14:53:52
7	Colchicine (Myinfla)". I think that's the	14:54:03
8	pronunciation.	14:54:06
9	Q. Let's take a look at table 6, which is on	14:54:07
10	page 22.	14:54:10
11	A. Okay.	14:54:20
12	Q. And what does this table show?	14:54:21
13	A. It says, [As read] Details of Included	14:54:22
14	Studies in Patients with Acute Coronary Syndrome."	14:54:25
15	Q. And what are the two studies?	14:54:30
16	A. COLCOT and COPS.	14:54:32
17	Q. And what intervention does it describe for	14:54:38
18	COLCOT and for COPS?	14:54:40
19	A. For COLCOT, it says, [As read] Colchicine	14:54:45
20	.5-milligram once daily plus standard care.	14:54:49
21	And for COPS, it says, [As read] Colchicine	14:54:53
22	.5-milligram twice daily for one month, then	14:54:55

1	.5-milligram once daily for 11 months in addition to	14:54:59
2	standard care.	14:55:02
3	Q. Okay. Let's look at table 7. What does	14:55:03
4	this table show?	14:55:08
5	What are the two studies that are identified	14:55:10
6	here?	14:55:12
7	A. LoDoCo 2 and LoDoCo.	14:55:12
8	Q. And what intervention does it describe for	14:55:16
9	LoDoCo 2 and LoDoCo 1?	14:55:19
10	A. For LoDoCo 2, it says, [As read] Colchicine	14:55:22
11	.5-milligram once daily plus standard care.	14:55:25
12	And for LoDoCo, it says, [As read]	14:55:27
13	Colchicine .5-milligram once daily plus standard	14:55:29
14	care.	14:55:32
15	Q. So LoDoCo is only 0.5 milligrams per day; is	14:55:33
16	that correct?	14:55:39
17	A. Yes.	14:55:39
18	Q. And there's no loading dose?	14:55:40
19	A. Correct.	14:55:43
20	Q. So I'm handing you a copy of Exhibit 1052.	14:55:43
21	(Exhibit 1052 was marked for	14:55:43
22	identification and was retained by counsel.)	14:56:03

1	Q. And what is it titled?	14:56:03
2	A. It says, "CADTH Reimbursement Review,	14:56:06
3	Stakeholder Feedback on Draft Recommendation."	14:56:10
4	Q. So on page 2 at the top of the page, it	14:56:29
5	states, [As read] Despite their smaller sizes,	14:57:12
6	LoDoCo and COPS also support COLCOT and LoDoCo 2.	14:57:15
7	Do you see that?	14:57:20
8	A. No, I don't. Where are you reading?	14:57:20
9	Q. On page 2.	14:57:23
10	A. Yeah.	14:57:24
11	Q. At the paragraph that's bridging page 1 and	14:57:25
12	page 2 at the concluding sentence.	14:57:32
13	"Despite their smaller sizes ..."	14:57:41
14	Does that?	14:57:43
15	MR. WILKERSON: Are you referring to page 1	14:57:44
16	of the PDF or page 1 of the internal document?	14:57:47
17	MR. LAURENCE: Page 2 of the PDF -- excuse	14:57:50
18	me. Page 3 of the PDF. Page 2 of the internal	14:57:53
19	document.	14:57:56
20	A. Okay. Now I see it, yes.	14:57:56
21	BY MR. LAURENCE:	14:57:59
22	Q. So what does that mean?	14:57:59

1	A. The last sentence saying, [As read] Despite	14:58:02
2	their smaller sizes, LoDoCo 2 and COPS also support	14:58:06
3	COLCOT and LoDoCo 2.	14:58:10
4	Right?	14:58:12
5	Q. Can you elaborate?	14:58:13
6	MR. WILKERSON: Objection to form.	14:58:14
7	Q. What do you think that means?	14:58:16
8	MR. WILKERSON: Same objection.	14:58:17
9	A. Well, I have to read the whole -- you know,	14:58:20
10	that whole section to give you -- give you or tell	14:58:22
11	you what they mean. I'm not the author of this	14:58:29
12	document, so I have to, basically, tell you what I	14:58:34
13	think the authors mean. They're just saying that	14:58:37
14	LoDoCo and COPS suggest that colchicine may have	14:58:40
15	beneficial effects in patients with coronary	14:58:47
16	disease.	14:58:51
17	Q. Could you turn to page 5 of the internal	14:58:54
18	document, page 6 of the exhibit? And then can you	14:58:56
19	see the name of the practitioner that's listed there	14:59:09
20	under C, "New Or Updated Conflict of Interest	14:59:14
21	Declarations"?	14:59:17
22	A. Yes.	14:59:18

1	Q. And who is listed there?	14:59:19
2	A. It says Jean-Claude Tardif, M.D.	14:59:20
3	Q. And what does that mean?	14:59:30
4	MR. WILKERSON: Objection. Form.	14:59:31
5	Q. Is that the listed inventor of the	14:59:34
6	'063 patent?	14:59:36
7	A. Yes.	14:59:37
8	Q. And can you turn to page 2 of the exhibit,	14:59:52
9	page 1 of the internal document? And look at the	14:59:57
10	sentence that appears toward the bottom of the page.	15:00:03
11	It's numbered 1. It states, [As read] The results	15:00:08
12	of the large trials, COLCOT and LoDoCo 2, are robust	15:00:10
13	and fully aligned. The reductions in the primary	15:00:15
14	efficacy end point with colchicine compared to	15:00:18
15	placebo are large, 23 percent and 31 percent in	15:00:22
16	COLCOT and LoDoCo 2 respectively, statistically	15:00:27
17	significant and have rarely been observed when	15:00:31
18	tested in addition to excellent standard care.	15:00:36
19	What does that sentence mean?	15:00:38
20	MR. WILKERSON: Objection to form.	15:00:40
21	Q. Those two sentences?	15:00:47
22	MR. WILKERSON: Same objection.	15:00:48

1 A. So what they're saying is that the two large
2 studies, COLCOT and LoDoCo 2, they show that there
3 is a significant reduction in primary cardiovascular
4 end points and that they were -- the difference was
5 statistically significant, and this was on top of
6 the standard care, so these effects are rarely
7 observed with many other drugs that have been
8 tested.

9 Q. And do you agree with those two sentences?

10 MR. WILKERSON: Objection to form.

11 A. I think, based on what I am seeing,
12 colchicine appears to be a very effective drug in
13 patients with coronary disease, and that's something
14 that I think is -- you know, the studies suggest
15 that it has beneficial effects in these patients.

16 Q. Do you agree with the sentence that appears
17 at the top of page 4 of Exhibit 1052, page 3
18 internally that's numbered at the top of page
19 number 1, where it --

20 A. You said page 1?

21 Q. Page 4 from the exhibit.

22 A. Okay.

1	Q. And page 3 internally, 3 of 11.	15:02:35
2	A. Yes.	15:02:38
3	Q. Do you agree with the sentence that appears	15:02:38
4	at the top of the page, and I'll read it, [As read]	15:02:40
5	The COLCOT and LoDoCo 2 trials have included more	15:02:42
6	than 10,000 patients, followed for a mean of more	15:02:45
7	than two years and extending up to five years, which	15:02:49
8	do not qualify as short-duration studies. The	15:02:52
9	durations of the pivotal and supportive	15:02:55
10	cardiovascular trials for colchicine 0.5 milligrams	15:02:59
11	daily are generally consistent with those of the	15:03:04
12	landmark statin trials which also range from 2 to	15:03:05
13	5 years in duration?	15:03:10
14	A. Do I agree with that?	15:03:11
15	Q. Yes.	15:03:12
16	A. Yeah, I think that's a fair statement. I	15:03:13
17	mean, LoDoCo 2 and COLCOT were in different groups	15:03:17
18	of patients, but I think the statement is fair.	15:03:20
19	Q. So is it fair to say, based on what you've	15:03:37
20	read, that Dr. Tardif has relied on COLCOT,	15:03:40
21	LoDoCo 1, LoDoCo 2, and COPS?	15:03:46
22	MR. WILKERSON: Objection. Form.	15:03:48

1	A. Dr. Tardif?	15:03:53
2	Q. Dr. Tardif and the company that is behind	15:03:54
3	sponsoring this colchicine Myinfla submission?	15:04:01
4	MR. WILKERSON: Objection to form.	15:04:06
5	A. I don't know where you got Dr. Tardif. It's	15:04:11
6	basically -- this appears to be from Pendopharm,	15:04:15
7	which is a division of Pharmascience.	15:04:21
8	Q. But on page 5 --	15:04:24
9	A. Yes.	15:04:27
10	Q. -- the information that's listed for the	15:04:28
11	declaration for the clinician 1 is Dr. Tardif.	15:04:31
12	A. Right. It's asking for conflict of	15:04:36
13	interest.	15:04:39
14	Q. Uh-huh.	15:04:39
15	A. So but the document is from Pendopharm.	15:04:40
16	Q. Well, on page 1 --	15:04:46
17	A. Right.	15:04:49
18	Q. -- it starts with, [As read] As lead	15:04:49
19	clinical researchers in the pursuit of new therapies	15:04:52
20	for secondary prevention of coronary disease who are	15:04:56
21	familiar with the evidence of efficacy and safety of	15:04:59
22	low-dose colchicine, we believe that the committee's	15:05:02

1 recommendation not to reimburse colchicine 15:05:05

2 0.5 milligrams daily for this purpose is not fully 15:05:09

3 taken into account the scope of the available 15:05:13

4 evidence it was provided. 15:05:15

5 So Dr. Tardif is one of the clinical 15:05:17

6 researchers that's listed in this document starting 15:05:23

7 on page 5; is that correct? 15:05:26

8 MR. WILKERSON: Objection to form. 15:05:28

9 A. Well, I don't think I agree with that. It 15:05:33

10 just says new or updated conflict of interest 15:05:35

11 declaration and his name is there. Whether or not 15:05:39

12 he is one of the primary authors of this document, I 15:05:41

13 can't tell you. This is -- this appears to be 15:05:46

14 coming from Pendopharm, and Pendopharm or whoever 15:05:49

15 authored this relied on those four clinical studies. 15:05:54

16 That's the extent of what I can tell you. Whether 15:05:58

17 or not Dr. Tardif relied on those four clinical 15:06:02

18 studies, you should ask him. 15:06:04

19 Q. Does Dr. Tardif work with Pendopharm or 15:06:08

20 Pharmascience? 15:06:11

21 MR. WILKERSON: Objection. Form. 15:06:12

22 A. Well, based on what you showed me on page 5, 15:06:15

1 it says that Dr. Tardif has a new or updated
2 conflict of interest declaration, and he says that
3 he has 5,001 to \$10,000 relationship with
4 Pendopharm. So that's the extent of what I can tell
5 you.

6 Q. So assuming that Dr. Tardif is one of the
7 clinicians that was involved in giving this feedback
8 in this document, is it safe to assume that he
9 embraces the teachings of those four studies --

10 MR. WILKERSON: Objection. Form.

11 Q. -- since he relied on them?

12 MR. WILKERSON: Objection. Form.

13 A. If he was the author of this document, all I
14 can tell you is that he's saying that the COLCOT and
15 LoDoCo 2 trials have included more than 10,000
16 patients followed for a mean of more than 2 years
17 and extending up to 5 years, which do not qualify as
18 short-duration studies. The durations of the
19 pivotal and supportive cardiovascular trials for
20 colchicine .5 milligram daily are generally
21 consistent with those of landmark statin trials,
22 which also range from 2 to 5 years in duration. And

1 I agree with that statement, too. 15:07:51

2 Q. Okay. And do you see, at the bottom of 15:08:00
3 page 1 of 11 of the internal document numbering and 15:08:04
4 page 2 of the exhibit, the sentence right before the 15:08:08
5 numbered paragraph that's numbered 1, where it says, 15:08:15
6 [As read] We are suggesting that CADTH reconsider 15:08:18
7 its draft recommendation not to reimburse this 15:08:22
8 low-dose preparation of colchicine based on the 15:08:25
9 following points. 15:08:27

10 And then it relies on -- makes points that 15:08:28
11 relied upon and cite to COLCOT and LoDoCo 2 in 15:08:32
12 paragraph numbered 1 and then LoDoCo and COPS in the 15:08:43
13 concluding sentence of that same paragraph. Do you 15:08:46
14 agree that that's what is there? 15:08:52

15 MR. WILKERSON: Objection to form. 15:08:53

16 A. Well, it's relying mostly on COLCOT and 15:08:56
17 LoDoCo 2, and then it's saying that, despite their 15:08:59
18 small sizes, LoDoCo and COPS also support COLCOT and 15:09:03
19 LoDoCo 2. So I think those are fair statements. I 15:09:07
20 don't see why that there is anything wrong with 15:09:13
21 them. 15:09:15

22 Q. Okay. 15:09:16

1	MR. LAURENCE: Let's take a break for a	15:09:18
2	minute.	15:09:20
3	THE VIDEOGRAPHER: Going off the record at	15:09:20
4	3:08 p.m.	15:09:24
5	(A short break was had.)	15:23:03
6	THE VIDEOGRAPHER: Going back on the record	15:23:04
7	at 3:22 p.m.	15:23:06
8	BY MR. LAURENCE:	15:23:08
9	Q. Dr. Tardif, you mentioned you were seeing an	15:23:10
10	increase in pericarditis after COVID?	15:23:13
11	A. I think you referred to me as Dr. Tardif.	15:23:16
12	Q. I'm sorry. Dr. Ardehali.	15:23:18
13	A. I would say we have seen many patients who	15:23:20
14	come in with ongoing chest pain, and they seem to	15:23:24
15	be -- they seem to be some kind of respiratory	15:23:29
16	component to it so we check for pericarditis in	15:23:33
17	those patients.	15:23:36
18	Q. And is pericarditis caused by an infection?	15:23:36
19	A. Not always, no.	15:23:41
20	Q. What is the basis for it in most	15:23:42
21	circumstances?	15:23:47
22	MR. WILKERSON: Objection to form.	15:23:49

1 A. To be honest, we don't understand many
2 cases, why they get pericarditis. It can be an
3 immune reaction or it can be an infection, either a
4 viral or bacterial.

5 Q. In the three documents we looked at from
6 submissions to the Canadian Agency for Drugs and
7 Technologies and Health, which is -- which is the --
8 and the acronym is CADTH, Exhibits 1051 through
9 1053, is it your understanding, based on those three
10 exhibits, that Pharmascience is pointing to four
11 studies, the COLCOT, LoDoCo 1, LoDoCo 2, and COPS
12 studies, in support of seeking reimbursement for the
13 use of colchicine?

14 MR. WILKERSON: Objection. Form.

15 A. Well, I haven't read all of these documents.
16 It was just, you know, I had not seen them before.
17 These are very thick documents, and there is a lot
18 of information there.

19 Based on those paragraphs that you showed me
20 I can tell you that it looks like they are mostly
21 relying on COLCOT and LoDoCo 2 and are saying that
22 LoDoCo and COPS supports the findings in the other

1	two studies.	15:25:31
2	Q. And in those paragraphs that you read, not	15:25:32
3	the ones that you haven't had a chance to read, is	15:25:36
4	it accurate to say that Pharmascience did not point	15:25:40
5	to the Bouabdallaoui paper?	15:25:43
6	MR. WILKERSON: Objection. Form.	15:25:45
7	A. I didn't see a reference to that paper in	15:25:47
8	what I -- what you showed me, no.	15:25:50
9	MR. LAURENCE: Let's pause off the record	15:26:05
10	for a moment.	15:26:06
11	THE VIDEOGRAPHER: Going off the record at	15:26:07
12	3:25 p.m.	15:26:09
13	(A short break was had.)	15:26:10
14	THE VIDEOGRAPHER: Going back on the record	15:27:04
15	at 3:26 p.m.	15:27:17
16	BY MR. LAURENCE:	15:27:18
17	Q. Dr. Ardehali, turning back to Exhibit 1057?	15:27:21
18	A. Okay.	15:27:41
19	Q. Earlier today you said, more than once, that	15:27:41
20	you aren't -- that -- you indicated that there was	15:27:45
21	not FDA approval for colchicine; is that correct?	15:27:49
22	MR. WILKERSON: Objection. Form.	15:27:53

1	A. I said there was no FDA approval for	15:27:55
2	colchicine for -- in patients with acute myocardial	15:28:00
3	infarction.	15:28:06
4	Q. So was this new information that was	15:28:06
5	contained in this Exhibit 1057 for you?	15:28:10
6	A. No. So this is not in patients with acute	15:28:14
7	myocardial infarction. These are patients with risk	15:28:17
8	factors for cardiovascular disease.	15:28:20
9	Q. Were you surprised that the FDA label for	15:28:27
10	LoDoCo doesn't include any limitations on colchicine	15:28:31
11	being administered within any particular time	15:28:37
12	period?	15:28:41
13	MR. WILKERSON: Objection to form.	15:28:42
14	A. Well, again, this is in patients with	15:28:45
15	cardiovascular disease, this is not in patients	15:28:52
16	after myocardial infarction.	15:28:54
17	Q. Well, could you look at the top of page 2?	15:28:56
18	A. Of the same document?	15:29:00
19	Q. Yes.	15:29:01
20	A. Okay.	15:29:07
21	Q. If you could read that sentence.	15:29:08
22	A. Which sentence?	15:29:10

1 Q. Where -- under numeral 1. 15:29:12

2 A. Right. So it says, [As read] Indications 15:29:15

3 and usage. LoDoCo is indicated to reduce the risk 15:29:17

4 of myocardial infarction (MI), stroke, coronary 15:29:21

5 revascularization, and cardiovascular death in adult 15:29:25

6 patients with established atherosclerotic disease or 15:29:30

7 with multiple risk factors for cardiovascular 15:29:35

8 disease. 15:29:40

9 Q. Okay. Is what you said earlier correct in 15:29:40

10 terms of the label that relates to colchicine? 15:29:43

11 A. Yeah. Again, this label is not for patients 15:29:48

12 who had myocardial infarction and underwent 15:29:51

13 angioplasty. These are patients with established 15:29:54

14 atherosclerotic disease, and it's not referring to 15:29:58

15 established atherosclerotic disease in the coronary 15:30:04

16 vessels. It's just talking about atherosclerotic 15:30:07

17 disease and/or they have multiple risk factors for 15:30:09

18 cardiovascular disease. 15:30:12

19 Q. And what are those risk factors? 15:30:13

20 A. So the risk factors for cardiovascular 15:30:15

21 disease are multiple. They include family history, 15:30:18

22 smoking, high blood pressure, diabetes, high 15:30:24

1	cholesterol. We know that patients who have	15:30:29
2	obesity, you know, low physical activity, you know,	15:30:36
3	those are less of risk factors. Age, age is	15:30:39
4	probably the biggest risk factor for cardiovascular	15:30:43
5	disease.	15:30:46
6	Q. So would a prior myocardial infarction be a	15:30:48
7	risk factor?	15:31:04
8	A. For another myocardial infarction?	15:31:07
9	Q. Correct.	15:31:10
10	A. Yes.	15:31:11
11	Q. Let's -- I'm handing you a copy of	15:31:15
12	Exhibit 1049 which is the declaration of Dr. Ridker.	15:31:54
13	(Exhibit 1049 was marked for	15:32:03
14	identification and was retained by counsel.)	15:32:05
15	Q. And if you could go to the very last page,	15:32:05
16	and turn to paragraph 249.	15:32:15
17	A. Yes.	15:32:19
18	Q. And then compare that paragraph with the	15:32:20
19	closing paragraph of your declaration -- in your	15:32:30
20	second declaration, which is paragraph 39.	15:32:39
21	A. I'm sorry. The first one or the second one?	15:32:42
22	Q. The second declaration is the one that has	15:32:45

1 paragraph 39 as the last paragraph. But I'm also 15:32:50
2 going to refer you to paragraph 61 of your first 15:32:53
3 declaration, which is identical to paragraph 39 of 15:33:10
4 your second declaration. If you could read those 15:33:18
5 paragraphs, and tell me what is different in his 15:33:22
6 closing paragraph relative to yours. 15:33:25

7 MR. WILKERSON: Objection to form. 15:33:28

8 A. Maybe I should start with the paragraph in 15:33:29
9 my first declaration. It says, [As read] This 15:33:33
10 declaration is based on information known to me as 15:33:35
11 of the date I signed this declaration, and I reserve 15:33:38
12 the right to amend or supplement this declaration in 15:33:42
13 view of any additional discovery documents, 15:33:45
14 information, declarations, and/or testimony that I 15:33:48
15 received after issuance of this declaration. I also 15:33:52
16 reserve the right to rebut opinions and testimony 15:33:57
17 offered by witness for petitioner. 15:34:00

18 Q. So let me break this down a little bit more 15:34:03
19 than my initial question. 15:34:05

20 Is your paragraph 61 in your first 15:34:08
21 declaration identical to paragraph 39 in your second 15:34:11
22 declaration? 15:34:14

1	A. Yes.	15:34:29
2	Q. And can you identify what's different	15:34:30
3	between your closing paragraphs that we just looked	15:34:37
4	at and the closing paragraph in Dr. Ridker's	15:34:40
5	declaration?	15:34:42
6	A. So --	15:34:46
7	MR. WILKERSON: Objection to form.	15:34:47
8	A. -- he wrote that, [As read] I declare that	15:34:48
9	all statements made herein of my knowledge are true	15:34:50
10	and that all statements made on information and	15:34:54
11	belief are believed to be true. I further declare	15:35:06
12	that all statements made herein were made with the	15:35:02
13	knowledge that willful false statements and the like	15:35:06
14	are punishable by fine or imprisonment or both under	15:35:10
15	section 1001 of title 18 of the United States Code.	15:35:15
16	Q. Is it correct that your declaration doesn't	15:35:19
17	conclude with a statement that you're willing to be	15:35:23
18	fined or imprisoned or both for false statements?	15:35:28
19	MR. WILKERSON: Objection to form.	15:35:33
20	A. Yeah, I don't have that in my conclusion.	15:35:40
21	Q. After each break or -- after each break, did	15:35:42
22	you discuss the substance of your testimony with	15:35:52

1	counsel or anyone else?	15:35:54
2	A. No. I -- he just told me, you know, I was	15:35:56
3	doing great and that's it.	15:36:01
4	Q. Okay.	15:36:03
5	MR. LAURENCE: No further questions.	15:36:05
6	MR. WILKERSON: Can we go off the record for	15:36:08
7	a short break?	15:36:10
8	MR. LAURENCE: Yep.	15:36:12
9	THE VIDEOGRAPHER: Going off the record at	15:36:13
10	3:35 p.m.	15:36:14
11	(A short break was had.)	15:36:15
12	THE VIDEOGRAPHER: Going back on the record	15:46:17
13	at 3:45 p.m.	15:46:29
14	EXAMINATION	15:46:32
15	BY MR. WILKERSON:	15:46:33
16	Q. All right. Dr. Ardehali, welcome back.	15:46:33
17	Just a couple questions from me.	15:46:36
18	Do you recall earlier, counsel had some	15:46:38
19	questions for you regarding inventorship of your	15:46:43
20	patents?	15:46:48
21	A. Yes.	15:46:48
22	Q. Are you a lawyer?	15:46:48

1	A. No.	15:46:49
2	Q. And are you an experienced patent lawyer?	15:46:50
3	A. No.	15:46:54
4	Q. And in obtaining your patents, have you	15:46:54
5	relied on the assistance of counsel?	15:46:58
6	A. Yes. We do have a patent office, and we	15:47:01
7	have lawyers at Northwestern.	15:47:05
8	Q. Okay. Can you go back to Exhibit 1057. And	15:47:06
9	that is the LoDoCo label.	15:47:21
10	A. Okay.	15:47:25
11	Q. You recall counsel asked you some questions	15:47:26
12	about this label earlier today?	15:47:30
13	A. Yes.	15:47:32
14	Q. Okay. Midway through on this cover page on	15:47:33
15	the right-hand side, do you see where it says	15:47:35
16	"Revised" and then there's a date?	15:47:39
17	A. Yes.	15:47:40
18	Q. Okay. What is the date listed?	15:47:40
19	A. 06/2023.	15:47:42
20	Q. Do you understand that to mean June of 2023?	15:47:45
21	A. Yes.	15:47:49
22	Q. Okay. And I'm sure you have all the	15:47:49

1	documents, but do you have the '063 patent?	15:48:01
2	I don't even know if I have it.	15:48:05
3	A. Yes.	15:48:07
4	Q. Okay. And that's Exhibit 1001; is that	15:48:07
5	right?	15:48:11
6	A. Yes.	15:48:11
7	Q. Okay. And do you see on the left hand of	15:48:11
8	the cover, it says, "Related U.S. Application Data?	15:48:18
9	A. Yes.	15:48:32
10	Q. Okay. And do you see there's two	15:48:33
11	provisional applications listed there, the '988 and	15:48:36
12	the '865?	15:48:40
13	Do you see that?	15:48:42
14	A. Yes.	15:48:42
15	Q. What are the two dates for those files?	15:48:42
16	A. For '988 -- I'm sorry. '988 is filed on	15:48:44
17	October 20, 2020. For '856 is November 15, 2019.	15:48:47
18	Q. Okay. And then a little bit above that, do	15:48:52
19	you see the date that the application that matured	15:48:56
20	into the '063 was filed there?	15:48:59
21	A. Yes.	15:49:02
22	Q. And what's that date?	15:49:03

1	A. It says, "Filed November 13, 2020."	15:49:05
2	Q. Okay. So all three of those dates are	15:49:08
3	before the date you just read on the LoDoCo label;	15:49:11
4	is that right?	15:49:15
5	A. Yes.	15:49:15
6	Q. Okay. Counsel also discussed the use of	15:49:16
7	colchicine in the prior art.	15:49:21
8	Do you remember that?	15:49:23
9	A. Yes.	15:49:24
10	Q. And there was a product previously approved	15:49:25
11	and a label for that product; is that right?	15:49:29
12	A. Yes.	15:49:32
13	Q. Okay.	15:49:32
14	MR. LAURENCE: Objection to form.	15:49:34
15	Q. I'm gonna hand you Exhibit 1016.	15:49:36
16	(Exhibit 1016 was marked for	15:49:36
17	identification and was retained by counsel.)	15:49:46
18	Q. And, Dr. Ardehali, do you recognize this	15:49:46
19	document?	15:49:50
20	A. Yes.	15:49:51
21	Q. Okay. What is it?	15:49:51
22	A. It's the FDA label for Colcrlys, which is	15:49:52

1	colchicine.	15:50:04
2	Q. Okay. And if you look at the middle on the	15:50:04
3	right-hand side of this page, do you see it says	15:50:07
4	"Revised," and then there's a date?	15:50:09
5	A. Yes.	15:50:11
6	Q. What is the date listed there?	15:50:11
7	A. 7/2009, July of 20 -- 2009.	15:50:12
8	Q. Okay. And do you recall earlier, counsel	15:50:17
9	asked you regarding the indications and the dosage	15:50:19
10	of Colcrys?	15:50:22
11	A. Yes.	15:50:24
12	Q. And for each of the approved indications,	15:50:24
13	what is the dosage for colchicine?	15:50:31
14	A. So for [As read] Gout flares, 1.2 milligrams	15:50:38
15	(two tablets) at the first sign of a gout flare	15:50:43
16	followed by 0.6 milligrams (one tablet) one hour	15:50:44
17	later.	15:50:44
18	For FMF, which is Familial Mediterranean	15:50:48
19	Fever, [As read] Adults and children older than	15:50:53
20	12 years, 1.2 to 2.4 milligram. Children 6 to	15:50:55
21	12 years, .9 to 1.8 milligram. Children 4 to	15:51:00
22	6 years, 0.3 to 1.8 milligram. Give total daily	15:51:03

1 dose in one or two divided doses. Increase or 15:51:08
2 decrease the dose as indicated and as tolerated in 15:51:12
3 increments of .3-milligram per day. Not to exceed 15:51:15
4 the maximum recommendation daily dose. 15:51:19

5 Yeah. 15:51:23

6 Q. And what's the dosage when colchicine is 15:51:23
7 administered to treat pericarditis? 15:51:29

8 A. I don't see it here. But usually, we give, 15:51:31
9 you know, 1.2 milligrams and then for several days. 15:51:38
10 Sometimes, again, we go for months. And then we go 15:51:44
11 down to .6 milligrams for maintenance. 15:51:46

12 Q. Okay. And so each of those instances from 15:51:49
13 the usage that was before the '063 patent have a 15:51:53
14 loading dose; is that right? 15:51:58

15 A. Pretty much, yes. 15:52:00

16 Q. Okay. And earlier, you testified that it 15:52:01
17 was important that the '063 patent explicitly 15:52:06
18 directs the exclusion of a loading dose. 15:52:10

19 Do you remember that? 15:52:11

20 A. Yes. 15:52:12

21 Q. Okay. Can you explain? Can you explain why 15:52:12
22 that's important? 15:52:18

1 A. Yes. So again, as physicians, we always -- 15:52:20
2 we, basically, load colchicine in almost every 15:52:26
3 indication we use it for because we want to inhibit 15:52:30
4 or suppress the inflammatory condition that is going 15:52:34
5 on. So what was discovered in COLCOT is that not 15:52:38
6 giving a loading dose is a big step forward because 15:52:46
7 this is like now I -- you know, if we use it after 15:52:50
8 myocardial infarction in patients who receive 15:52:56
9 angioplasty, we don't give a loading dose. So this 15:52:58
10 is like an indication where I would tell the team, 15:53:03
11 you know, my trainees make sure you don't give a 15:53:06
12 loading dose because we use it in almost every other 15:53:09
13 condition we give a loading dose. 15:53:13

14 Q. Okay. And what would a POA expect or take 15:53:15
15 away from a clinical trial that came after the 15:53:25
16 Colcrys label that was silent on a loading dose? 15:53:33

17 MR. LAURENCE: Objection. Leading. 15:53:36

18 A. So, basically, if it doesn't say that a 15:53:37
19 loading dose was -- you know, that they didn't use a 15:53:39
20 loading dose, it's not excluding it. It's just 15:53:40
21 saying that the loading dose was not used in the 15:53:43
22 clinical trial. 15:53:46

Transcript of Hossein Ardehali, M.D.
Conducted on June 18, 2024

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1	Q. Okay.	15:53:47
2	MR. WILKERSON: All right. No further	15:53:54
3	questions.	15:53:55
4	MR. LAURENCE: No further questions.	15:54:10
5	THE VIDEOGRAPHER: This marks the end of the	15:54:12
6	deposition of Dr. Hossein Ardehali. We are going	15:54:14
7	off the record at 3:53 p.m.	15:54:17
8	(Off the record at 3:54 p.m.)	15:54:20
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CERTIFICATE OF COURT REPORTER - NOTARY PUBLIC

I, TIFFANY M. PIETRZYK, Certified Shorthand Reporter No. 084-004371, CSR, RPR, CRR, and a Notary Public within and for the State of Illinois, do hereby certify:

That HOSSEIN ARDEHALI, M.D., the witness whose deposition is hereinbefore set forth, was duly sworn by me before the commencement of such deposition and that such deposition was taken before me and is a true record of the testimony given by such witness.

I further certify that the adverse party, INSTITUT DE CARDIOLOGIE DE MONTREAL, was represented by counsel at the deposition.

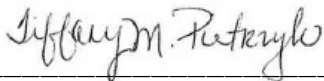
I further certify that the deposition of HOSSEIN ARDEHALI, M.D. occurred at the offices of ArentFox Schiff LLP, 233 South Wacker Drive, Suite 7100, Chicago, Illinois, on Tuesday June 18, 2024, commencing at 9:13 a.m. CST to 3:54 p.m. CST.

I further certify that I am not related to any of the parties to this action by blood or

1 marriage, I am not employed by or an attorney to any
2 of the parties to this action, and that I am in no
3 way interested, financially or otherwise, in the
4 outcome of this matter.

5 IN WITNESS WHEREOF, I have hereunto set my
6 hand and affixed my notarial seal this 21st day of
7 June, 2024.

8
9 My commission expires: February 28th, 2028

10
11 

12 NOTARY PUBLIC IN AND FOR THE
13 STATE OF ILLINOIS

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