

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MURRAY & POOLE ENTERPRISES, LTD.,
Petitioner,

v.

INSTITUT DE CARDIOLOGIE DE MONTREAL,
Patent Owner.

IPR2023-01064
Patent 11,400,063 B2

Record of Oral Hearing
Held: October 15, 2024

Before ULRIKE W. JENKS, SHERIDAN K. SNEDDEN, and
ZHENYU YANG, *Administrative Patent Judges*.

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The above-entitled matter came on for hearing on October 15, 2024, commencing at 1:00 p.m. EDT, at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia.

P R O C E E D I N G S

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JUDGE JENKS: Good afternoon and welcome to the USPTO office in Alexandria. We're convened for oral arguments in IPR2023-01064, which pertains to the patentability challenges of claims in US Patent No. 11,400,063. I'm Judge Jenks and I'm joined by Judges Yang and Snedden in the hearing room.

Let us get started with appearances for both parties, for those who will be arguing today, including any of these practitioners. If anyone else is attending in person or remotely with you today but will not be speaking, please identify them as well. For example, please state if your client is attending.

Following the hearing, please confer with the court reporter to ensure that there are no questions regarding any spelling of names or terms. We will start with the appearances for the petitioner.

MS. BROUGHER: Hello, Your Honor. My name is Joanna Brougher. I'm lead counsel for Petitioner Murray & Poole. I am joined today by my co-counsel, Matthew Phillips and Kevin Laurence from Laurence & Phillips.

JUDGE JENKS: Now for Patent Owner?

MR. PATEL: Good afternoon, Your Honor. My name is Sailesh Patel from ArentFox Schiff on behalf of the patent owner. With me is Matthew Wilkerson, who will also be arguing today. Also here is Kevin Nelson from ArentFox Schiff, and our client representative, Melanie Carpentier.

JUDGE JENKS: Thank you so much. So, before we begin, we

1 need to go over some ground rules. Recording of any PTAB hearing is
2 prohibited. The Court reporter will provide a transcript of the hearing that
3 will become part of the record and in the proceeding at a later date. To
4 ensure that the transcript of this hearing is clear, we ask you to speak directly
5 into the microphone when talking and to identify specific slide numbers or
6 any other pertinent identifying information when referring to
7 demonstratives.

8 We understand that every case that comes before us, the parties
9 have a lot at stake. To prepare for your oral arguments, we have
10 familiarized ourselves with the record and issues in the case. We have
11 reviewed the briefs and any evidence provided in the record, including
12 demonstratives, and have these documents available on our computers. We
13 remind the parties that Petitioner has the ultimate burden of establishing
14 unpatentability by a preponderance of evidence.

15 Per the hearing order paper 40, each party has 60 minutes, and
16 because each party also will rely on the presentation from the LEAP
17 practitioner, each side gets an additional 15 minutes of argument time,
18 providing a total of 75 minutes to argue their case. We remind the parties
19 that the LEAP practitioner must have a meaningful and substantive
20 opportunity to argue during the hearing today.

21 That said, there is no time requirement for that argument.
22 Petitioner will open the argument and may reserve rebuttal time, which may
23 not exceed more than half of Petitioner's total argument time. Patent Owner
24 will then respond to Petitioner's arguments and may reserve surrebuttal time,
25 also not to exceed more than half of Patent Owner's total argument time.

26 Please remember that your arguments should be limited to only

1 those arguments previously presented in your briefs. I just want to warn
2 everybody today that we will be taking a break during the hearing, and most
3 likely that break will occur after Petitioner's opening argument. Petitioner,
4 do you wish to reserve any rebuttal time?

5 MS. BROUGHER: Sure. I would like to reserve 30 minutes,
6 please.

7 JUDGE JENKS: 30 minutes. All right, excellent. Very good.
8 You may begin your arguments when ready.

9 MS. BROUGHER: Thank you, Your Honor. I did bring
10 additional copies of the demonstratives for the judges. Would you like a
11 handout?

12 JUDGE SNEDDEN: No, I won't need it. I'll just use what I have
13 on the computer here.

14 MS. BROUGHER: Thank you.

15 JUDGE JENKS: Oh, and please remember since I'm viewing it
16 remotely, I don't see your screen. So you will have to let me know every
17 time you change a slide so I can follow you.

18 MS. BROUGHER: Thank you. May it please the Board. A list of
19 the topics that we wish to discuss today are provided on slides 2 and 3. I
20 believe we put together a very comprehensive slide deck for you. So I'm
21 happy to take this discussion in any direction that you see fit, but I do
22 propose that we start with addressing Ground 2 as we view this the easiest to
23 decide upon.

24 But before I dive into Ground 2, I would like to begin by providing
25 a little bit of overview about the drug in discussion today because I think this
26 background will provide a good foundation of some of the issues that we're

1 going to be talking about today.

2 So, colchicine. Colchicine is the drug we're talking about today.
3 Colchicine is a very, very old drug. It has been around for centuries, dating
4 back to the ancient Greek and even ancient Egyptian times. It has
5 historically been used exclusively for the treatment of gout and FMF, which
6 is familial Mediterranean fever.

7 JUDGE JENKS: I'm sorry. I was just asked, could you turn your
8 microphone on? It's usually at the bottom there. There's an on-off button.

9 MS. BROUGHER: Is that better?

10 JUDGE JENKS: Oh, so much better.

11 MS. BROUGHER: All right. So back to colchicine and back to
12 gout. So gout and FMF are both very painful, acute inflammatory
13 conditions that result in swollen joints. In the context of gout, it appears as a
14 swollen big toe. In the context of FMF, it's just swollen joints all over your
15 body. But these are very painful acute conditions that typically resolve
16 themselves within a few days. So that's how colchicine has historically been
17 used.

18 Colchicine received its first FDA approval in 1961 as a
19 combination product for the treatment of gout. What's unique about that
20 1961 date is that it is one year prior to when the Kefauver-Harris
21 Amendments came into play with the FDA, which required that any drug
22 approved by the FDA be both safe and efficacious. So colchicine, in
23 essence, kind of got grandfathered in under the old FDA laws.

24 So in 2006, the FDA decided to go after these drugs that were
25 grandfathered in and required them to undergo additional testing so that they
26 could prove this efficacy requirement. So in 2007, colchicine underwent a

1 small clinical trial, less than 200 patients, where they showed that it was
2 both safe and efficacious.

3 I should also mention at this point that colchicine is a rather toxic
4 drug. It has side effects ranging from anything from gastrointestinal issues,
5 such as diarrhea, to much more severe issues, such as death. So during this
6 trial in 2007, they tried a shortened and a reduced dosage regimen for
7 colchicine, and they proved that it worked. And they were able to apply and
8 receive FDA approval in 2009 under the name of Colcris.

9 And this label, which is shown here on slide 4, actually has the
10 indications, both gout and FMF, as well as the warnings and
11 contraindications that came out of this study.

12 So up until about 2008, colchicine has been used almost
13 exclusively for the treatment of gout and FMF. Well, in 2008, Dr. Mark
14 Nidorf, a cardiologist in Australia, decided to see if colchicine will work in
15 his patient population, namely patients with stable coronary artery disease.
16 So I'm going to pause for one moment and explain what coronary artery
17 disease is, because I think this is important in understanding the indications
18 that we're talking about today.

19 So coronary artery disease is a disease of the arteries that comes
20 directly from the name. But more specifically, it involves the formation of
21 plaques within the arteries. And this plaque formation is called
22 atherosclerosis. These plaques could break off, and they could also then
23 travel through the blood to the brain and cause a stroke, or they can travel to
24 the heart and cause a heart attack.

25 And so what Dr. Nidorf wanted to do is to see if having a drug like
26 colchicine that has these anti-inflammatory effects could play a role in

1 atherosclerosis. Now, I will stop here and say that atherosclerosis, the
2 condition we're talking about, is not gout. It is not FMF. Both of those are
3 conditions that involve acute, painful swelling of the joints. And it's also not
4 pericarditis. Pericarditis is an inflammation of the pericardium, which is the
5 sac that holds the heart. And pericarditis is typically resulted from a
6 bacterial or viral infection.

7 So again, not the same thing that we're talking about here with
8 coronary artery disease and this buildup of plaques. So Mark Nidorf ran this
9 trial. This is known as the LoDoCo Trial. And this was the first time that
10 somebody showed that targeting inflammation can play a role in reducing
11 cardiovascular events. So this is what the study is known for.

12 And some of the results that we had here was a reduction in acute
13 coronary syndrome, out-of-hospital cardiac arrest, and also stroke. And I
14 mention stroke because that comes into play with round II. Mark Nidorf
15 later confirmed the results of LoDoCo1 in the LoDoCo2 trial, which was a
16 bigger trial. It was placebo-controlled. But it confirmed the findings of
17 LoDoCo1.

18 LoDoCo was approved by the FDA last summer, or the summer of
19 2023, sorry. And it is owned by Petitioner Murray & Poole. And I have had
20 the pleasure of working on that patent portfolio for over 10 years. All right.
21 So LoDoCo clearly was the groundbreaking study that really opened the
22 door for a lot of future studies looking at colchicine in the cardiovascular
23 space.

24 So turning to slide 6 now, one of the studies that followed in
25 LoDoCo's footsteps was the CANTOS trial. This was run by Novartis. It
26 did not involve colchicine. It involved one of their antibodies. And what

1 was so significant about CANTOS is that it targeted inflammation
2 specifically.

3 So back to our coronary artery disease, we know that
4 atherosclerosis has potentially many different factors that impact it. It can
5 be caused by a bad diet. It can be caused by high blood pressure, cholesterol
6 levels, and what we know now is inflammation. So we don't know with
7 LoDoCo, for instance, when the colchicine acted on atherosclerosis. We
8 don't know if it acted on purely atherosclerosis or if it had an impact perhaps
9 on blood pressure or on cholesterol levels.

10 So what CANTOS sought to do was it had a very specific
11 antibody, and that specific antibody targeted a very specific inflammatory
12 pathway. And CANTOS proved without doubt that you can affect
13 cardiovascular outcomes by just targeting inflammation and not any of these
14 other factors such as cholesterol or anything else.

15 Now cholesterol, as you know, is probably the number one way
16 that we are treating cardiovascular disease. Statins, if we think about it,
17 Lipitor, what's all over the news. Those target cholesterol with the hope that
18 it also affects cardiovascular events. But now with CANTOS we proved, or
19 Novartis I should say, proved that you can improve cardiovascular events by
20 just targeting inflammation.

21 So turning to slide 7, you see kind of the timeline here of all these
22 studies. And it all started with LoDoCo1. And a bunch of studies came
23 after LoDoCo1, including CANTOS, including some others, and they just
24 investigated different aspects of colchicine on cardiovascular disease. And
25 this brings us to the COLCOT trial, which forms at least part of the claims at
26 issue here and the patent that we're talking about.

1 So COLCOT, what COLCOT did was confirm the trials before it.
2 It had the same dosing regimen as LoDoCo. It tested the same results as
3 LoDoCo, which are these major adverse coronary events. The difference
4 here is that they shortened the time period to treatment initiation. With
5 LoDoCo, the patients were at least six months stable. CANTOS, they were
6 at least 30 days after some sort of an event. And COLCOT reduced that
7 time period to within 30 days.

8 The final study that I will point to before we turn over to Ground 2
9 is the Bouabdallaoui paper, and this is our Exhibit 1005. This is a post hoc
10 analysis of COLCOT. In other words, this is a purely statistical workup of
11 the COLCOT data, but this is the first time that we see these specific short
12 time periods of 0-3, 4-7, 8-30 days come in, and these are the limitations that
13 got added to the claims of this '063 Patent.

14 So on slide 10 is just the patent we're talking about here, plus its
15 independent claims. There are a number of limitations to these claims, but
16 we believe that the main limitations are these that are highlighted on slide 11
17 for Claims 1 and 8. We're talking about initiating within about 3 days of an
18 MI, and for Claim 27, we're talking about reducing the risk of a stroke.

19 So now, if there are no other questions, I will turn to Ground 2. So
20 Ground 2 is our anticipation ground. And on slide 14, you see the claim that
21 we're talking about here. This is Claim 27. And Claim 27 is anticipated by
22 the COLCOT protocol, what we call 1006. And just as a starting point, this
23 COLCOT protocol was a publicly accessible printed publication in time for
24 it to be prior art to the '063 Patent. Specifically, this was publicly accessible
25 on March 8, 2017.

26 If you look at the claim again, you'll notice that there's only one

1 active step in the claim, and that begins with the phrase initiating the
2 administration of colchicine. This is a standalone phrase in this claim. It
3 identifies the patient population, it identifies the treatment that these patients
4 are getting, and this also identifies the time of treatment that the -- well,
5 when the patients are receiving this.

6 So the body of the claim here is a body that stands alone without
7 any support from the preamble. But now if you look at the preamble,
8 reducing the risk of stroke, as Your Honors correctly pointed out in the
9 institution decision, this preamble should be construed as non-limiting.
10 Why? Because again, the body of the claim stands alone. It identifies the
11 patients, the treatment, and the time. So there's nothing in the preamble that
12 really breathes any light into the body of the claim.

13 There's also no prosecution that we can talk about where the
14 examiner actually identified any prior art over which that preamble had to
15 account for. And there's also nothing in that body of the claim that requires
16 any sort of efficacy. So the preamble should be construed as non-limiting.
17 But even if it is limiting, the COLCOT protocol, our Exhibit 1006,
18 inherently discloses this effect.

19 In other words, if you practice the steps of this claim, that one step
20 that we talked about, you will inevitably get risk reduction in stroke. And
21 we also knew that from LoDoCo several years prior. LoDoCo, remember,
22 found that there was a statistically significant reduction in stroke. Are there
23 any questions on Ground 2 before I turn to Ground 3?

24 JUDGE JENKS: I do not have any questions.

25 MS. BROUGHER: Thank you. So I will now turn to Slide 20,
26 which identifies Ground 3, which is our obviousness ground. So these are

1 the two claims at issue, Claims 1 and 8. Now, as you can see by this chart
2 on slide 22, all of the limitations of Claims 1 and 8 are taught by both the
3 Nidorf Patent and the COLCOT protocol, except for this within-three-day
4 limitation that I mentioned earlier. So that's what we're going to be focusing
5 on primarily today.

6 So looking at slide 23, again all claim limitations are taught by
7 Nidorf and COLCOT, except for this TTI of within three days of an MI. In
8 other words, it teaches without preloading. LoDoCo had no loading dose. If
9 it had a loading dose, it would have been expressly stated, and that is
10 confirmed by both Dr. Ridker and Dr. Ardehali.

11 Also, it was done following a PCI, which is a standard procedure
12 that patients who have a stroke or an MI undergo. So really the big question
13 here was about motivation to reduce TTI to within about three days of the
14 MI.

15 And as Your Honors correctly pointed out in the institution
16 decision, there is a presumption of obviousness when a claim range falls
17 within the claim range of the prior art reference, and that is correct. But
18 there's many other ways that we can also reduce this TTI to within about
19 three days. And it's not a giant leap because many references, including
20 Hennessy, which was before the examiner at that time, taught a reduced TTI
21 window. In Hennessy in particular, it was within seven days.

22 The only new evidence presented by Patent Owner is providing
23 several new articles, oftentimes without pinpoint citations, to try to allege
24 hindsight, teaching way, or unpredictability. But as we'll discuss, a lot of
25 these are just manufactured arguments that really point to references that
26 have nothing to do with the disease we're talking about here.

1 So unless there are questions specifically about the within pre-
2 loading or without pre-loading dose or the PCI limitation, I would like to
3 turn to the motivation. But I see there's a question.

4 JUDGE SNEDDEN: No, I don't have any question.

5 MS. BROUGHER: All right. So then I will turn to slide 32. So,
6 motivation to reduce TTI. As I mentioned, there is this obviousness
7 presumption when you're showing a range that falls within the range of the
8 prior art reference. So that's presumptively obvious. But we have at least
9 six other ways that we can get to this reduced TTI window.

10 First is a trend in the art, and we'll show that in a few slides. The
11 trend was already moving towards this reduced TTI window. There's also
12 routine optimization that we can talk about here. And this is simply when
13 you have a results-effective variable that you're optimizing. Also, these
14 specific time periods 0-3, 4-7, greater than 8 days, are well-known stages
15 that correspond to the usual journey of patients with MI.

16 So in other words, this is nothing more than taking known time
17 periods and overlaying them with the broader range that we already had
18 here. And just as a note, the 0-3 day time period refers to the time that
19 patients are still in the hospital. So it is, you know, common sense at this
20 point to initiate treatment for patients before they leave the hospital.

21 But then we also have the ESC Guidelines. Now, we'll talk about
22 the ESC Guidelines in a little bit, but the ESC Guidelines are the standard of
23 care for patients with an MI. They don't just talk about statin therapy. They
24 talk about a broad range of secondary therapies, including aspirin, beta-
25 blockers, ACE inhibitors, lipid-lowering agents, and a bunch of other ones.
26 So this really is the standard of care for patients.

1 And the ESC Guidelines are the ones that talk about reducing or
2 getting patients started on therapy before they leave the hospital. It's also
3 well known that starting patients on therapy before they leave the hospital
4 improves their treatment outcomes and also improves their compliance with
5 taking the drug, all of which kind of makes patients healthier at the end of
6 the day.

7 So here we have at least six or seven ways that we can reduce the
8 TTI window from within 30 days to within 0-3 days. And any one of these
9 alone should be sufficient to get us to this obviousness determination for this
10 reduced TTI window. But we have six here.

11 There's also a reasonable expectation of success to reduce TTI to
12 within three days, and Dr. Ridker went into this extensively in his
13 declaration as how a POSA would view all of this information to reach that
14 within about three day window. And MHI has not produced any evidence
15 since the institution decision that would suggest otherwise.

16 So now I would like to kind of continue with this thought about
17 how we are motivated to reduce our TTI. If we turn to slide 33, this is a
18 good place to start because it shows us what patients we're really focusing
19 on. So LoDoCo and COLCOT were both directed to stable patients.

20 So these are not patients who are presenting in the ER with an
21 active stroke or an active MI. Those patients get treated differently. Those
22 patients get treated where the surgeons have to unblock their arteries and
23 reperfuse them so that you can restore blood flow back to the brain or to the
24 heart.

25 So these are not those patients. These are patients who have
26 already gone. They're PCIs, and their blood flow has already been restored.

1 And these are patients who can be discharged from the hospital, and usually
2 they can be discharged at two to three days post-MI. This is not uncommon.
3 And Dr. Ridker discusses this in his first declaration.

4 Now, MHI incorrectly tries to argue that COLCOT nearly included
5 patients who were stable, but this is not the case. This is an actual quote
6 from Dr. Ardehali's first declaration where he admitted that the COLCOT
7 protocol and Nidorf both involved stable patients. But we also see this back
8 on slide 33 with the inclusion and exclusion criteria for COLCOT. So these
9 are stable patients. These are patients who are able to continue with their
10 treatment.

11 Now, slide 35 shows a timeline of the different trials that have
12 taken place, starting with the LoDoCo trial. And a number of other trials
13 have continued after LoDoCo. And each one of them looked at a reduced
14 time-to-treatment period. Deftereos, for instance, looked at within 12 hours
15 of an event. Hennessy, again which was before the judges, looked at within
16 seven days. So the trend was already moving towards finding that optimum
17 shorter window.

18 I'm going to skip slide 36 for a second and move on to slide 37,
19 which talks about reducing TTI through routine optimization. Now, we
20 know that colchicine works in stable patients. We knew that from LoDoCo.
21 We knew that from other studies. We also knew that it was safe when
22 initiated in early time periods. We knew that from Hennessy and Deftereos
23 and a number of other studies.

24 So in this situation, this is nothing more than just optimizing a
25 results-effective variable. We also -- back to the slide 37, this is also
26 supported by the ESC Guidelines, which say that secondary preventative

1 therapy should be initiated at day 2 or 3 post-MI. And we also know that
2 initiating secondary therapy, as shown on slide 38, is associated with better
3 outcomes as well as better patient compliance. And that comes also from
4 the ESC Guidelines as well as other resources out there.

5 Slide 39. We know that motivation to start secondary preventive
6 therapy is just due to the usual journey of patients with MI. So these time
7 periods that we talked about, these are well-known time periods in the art.
8 And this particular screenshot here comes from the Bouabdallaoui paper, but
9 it does reference other papers that predate it. So these are well-known time
10 periods.

11 Both Dr. Ardehali and Dr. Ridker on slide 40 agreed that initiating
12 secondary therapies should be started prior to hospital discharge. Again, it is
13 better to give patients their medicine before they go home and forget to go
14 pick up the medicine at CVS.

15 Now, the ESC Guidelines. There's been a lot of discussion about
16 whether or not these guidelines are even relevant here, but they are
17 extremely relevant. These literally are the standard of care for treating
18 patients with MI. There are also corresponding ESC Guidelines for the
19 treatment of pericarditis or other cardiovascular events. These in particular
20 though, teach a wide range of secondary therapies. So not just statins, but
21 also aspirin and other beta-blockers, ACE inhibitors.

22 They are also relevant because they are treating MI patients, the
23 same patients that we're talking about here. And they're looking at the same
24 time periods. So even though statins were common first-line treatments for
25 stable MI, these concepts that are here in the ESC Guidelines apply to all
26 secondary therapies, including colchicine.

1 Now I will turn back to the slide I skipped, which is slide 36.
2 There was also a reasonable expectation of success, as I mentioned before.
3 Low-dose colchicine was known to work in stable patients. And there was
4 no reason to think that this low-dose colchicine, which worked and was safe,
5 would somehow not work after stabilization.

6 And here's a great quote from Dr. Ridker on this point, saying how
7 following the success of LoDoCo and the COLCOT protocol, you know, a
8 person of ordinary skill in the art would have expected that colchicine would
9 work the sooner it got started.

10 Now I will turn to slide 42. So Patent Owner is trying to argue that
11 improved patient compliance requires hindsight. But as an initial matter,
12 this is a new surreply argument that was never previously raised. But even if
13 it was previously raised, it's irrelevant because we know from a number of
14 studies, including Deftereos, that starting low dose colchicine treatment
15 within 12 hours was safe. So we already knew that it was safe. There was
16 also no hindsight or teaching away or unpredictability, as Patent Owner
17 alleges.

18 Patent Owner provided a list of publications, mostly without any
19 pinpoint citations, to support their unpredictability argument. But quite
20 frankly, we don't know what point they're trying to make with these articles.
21 We did have Dr. Ridker on slide 44 take a look at these articles, and he
22 provided his assessment with it, and he grouped them into four different
23 categories.

24 The most relevant category includes LoDoCo, COLCOT, and
25 LoDoCo2. This is on slide 44. The other references all fall into different
26 categories, in particular in this category of surrogate endpoints that are really

1 targeting the acute phase and unstable patients.

2 So turning to slide 45, these references that Patent Owner tries to
3 assert as showing unpredictability in the art, these are all looking at
4 biomarkers of acute inflammation within 30 days, rather than what we care
5 about here, which is looking at the effect of colchicine on the disease which
6 or coronary artery disease.

7 And Patent Owner argues that a lack of effect in the acute phase
8 shows that colchicine is unpredictable. But this is not true because the
9 biologic processes that are at issue in the acute phase are different from the
10 biological processes that operate in the chronic phase. And this comes from
11 Dr. Ridker's first declaration as well as his second declaration.

12 So showing no effect in the acute phase means that colchicine
13 effect is really on chronic atherosclerosis, which is the LoDoCo trial. Are
14 there any questions on Ground 3?

15 JUDGE JENKS: I have no questions.

16 MS. BROUGHER: So now I will turn to objective indicia on slide
17 48. So we talked about Ground 3. We talked about obviousness. The '063
18 Patent can further not be saved by objective indicia because there are no
19 credible results here in the statistics section. These results are not expected,
20 they're not unexpected or otherwise. There's just simply no invention that
21 we can talk about here.

22 The claims at issue in the '063 Patent are based on a flawed post
23 hoc subgroup analysis that lacked any statistical power to make the
24 conclusions that they made in the '063 Patent. Subgroup analyses are
25 inherently flawed and unreliable, and Patent Owner didn't do any of the
26 things that Patent Owner could have done to try to make these data more

1 reliable.

2 So the Bouabdallaoui's assertions in 1005 of any sort of alleged
3 superiority of the 0-3 day time period are also biologically implausible. And
4 we have not yet received any sort of explanation for why they should be
5 plausible. So there's no biological plausibility behind any of these data.

6 As Paul Ridker said, to agree with these results is basically
7 agreeing that this drug somehow magically works between days 0-3, then
8 doesn't work again from days 4-7, then somehow magically works again at
9 some unknown time period. But all in all, we've already shown that this is a
10 drug that is meant to be given to patients on a long-term basis for two-plus
11 years. Those were the LoDoCo and the COLCOT trials. So there's no
12 explanation for why it magically does not work on days 4-7.

13 The same can be true for all the other time periods here, including
14 4-7, 8-30, 3-5, or any sort of permutation of these numbers. The data just
15 does not make sense, and it is nothing more than just a play of chance in
16 statistics.

17 Now, I'd like to point out that Patent Owner has never rebutted any
18 of our statistics arguments, any of the arguments made by Dr. Ridker, any of
19 the arguments made by Drs. Fiolet and Cornel in their publication, and
20 they've never provided their own assessment of the statistics. Dr. Ardehali
21 did not provide any statistics arguments. In fact, he admitted that he is not
22 an expert in statistics, and his knowledge of statistics comes from one
23 undergraduate class.

24 In contrast, Dr. Ridker has a very sophisticated level of
25 understanding of statistics, at least a master's degree in public health, and he
26 teaches epidemiology at the Harvard Medical School.

1 On slide 50, Patent Owner's only argument against the statistics is
2 to say that the mere fact that the data shows a benefit across 30 days and
3 within 3 days does not show that it defies biological plausibility. Rather, it
4 merely shows the data were insufficient to draw conclusions for specific
5 days between 8-30. But that's exactly the whole point of our argument, that
6 these time periods were never statistically powered to look at any of these
7 data. So you can't draw any sort of conclusions from them.

8 Moreover, there were more patients in the 8-30 day time period
9 than in the 0-3 day time period, more than double the size. And in statistics,
10 the more patients you have and the more data points you have, the more
11 reliable your numbers should be. But that's not the case here. So this really
12 goes to show you that statistically, the data that resulted in the TTI
13 limitations that we saw here is just not reliable.

14 Now, I am happy to go through the statistics arguments if you
15 wish, or we can move on to Ground 1.

16 JUDGE JENKS: You can go ahead and move on to Ground 1.

17 MS. BROUGHER: Thank you. So Grounds 1 and 4 both rely on
18 the Bouabdallaoui reference. On slide 62, you see the claims here at stake, 1
19 and 8, but the main issue here with Grounds 1 and 4 really comes down to
20 whether or not our reference 1005, the Bouabdallaoui paper, qualifies as
21 prior art. If it does qualify as prior art, it is invalidating under both
22 anticipation as well as obviousness. So that's the big question here, is this
23 prior art?

24 On slide 63, you see a timeline of everything that happened in this
25 case, or at least when the provisional applications were filed. So the first
26 provisional was filed in November 2019. The Bouabdallaoui paper was

1 published August 29, 2020, about eight months later. The second
2 provisional was filed October of 2020, and the non-provisional was filed
3 November of 2020.

4 Just as a starting point, these specific time periods that we're
5 talking about, 0-3, 4-7, all of those first appeared in the November 2020
6 non-provisional filing date. The provisional talked about other time periods.
7 It talked about 0-5, 0-10 days, 0-15, et cetera. But these specific time
8 periods that came out of the Bouabdallaoui paper first showed up in the non-
9 provisional filing of November 2020.

10 So then the question is, is this reference prior art by another? And
11 a starting point here is to look at the burdens in this case. And the burden-
12 shifting framework of Dynamic Drinkware applies. Petitioner has met its
13 initial burden of production, because the Bouabdallaoui paper is published as
14 the first author by Bouabdallaoui. And so on its face, the Bouabdallaoui
15 reference satisfies this burden of production.

16 Your Honors agreed while instituting trial, saying that this issue
17 will benefit from development during trial. So since the institution, this
18 burden of production has since been and continues to remain with Patent
19 Owner in this case. And Patent Owner should have produced sufficiently
20 corroborated evidence that the 0-3 day time limitation was solely conceived
21 by Dr. Tardif. If it was not solely conceived by Dr. Tardif, then it is prior art
22 by another.

23 And quite frankly, Patent Owner has not satisfied their burden of
24 production. What little evidence we have received actually suggests that
25 there are other inventors involved here. And I'm going to take you through
26 the evidence that we have received in this case.

1 First, as a starting point, this is on slide 65. The Bouabdallaoui
2 reference itself shows that Dr. Tardif is one of 24 authors. But Dr.
3 Bouabdallaoui is the first author. She's the one who interpreted the
4 statistician's findings, and she wrote the manuscript for what we're calling
5 the Bouabdallaoui paper.

6 Patent Owner has produced evidence in the form of Dr. Tardif's
7 declaration, Dr. Ardehali's declaration, as well as Bouabdallaoui declaration.
8 And we also have other evidence from Dr. Tardif's deposition as well as Dr.
9 Bouabdallaoui's deposition as well.

10 Now I'm going to walk you through this evidence. This is on slide
11 66. So there's a statement in Dr. Tardif's declaration that points to the
12 declaration that he signed when the patent application went through patent
13 prosecution. But this kind of goes both ways. It says that he is the original
14 inventor or a joint inventor.

15 On slide 67, in his declaration, he talked about how he designed
16 the COLCOT study, how he obtained the funding for the COLCOT study,
17 how he's the principal investigator of the COLCOT study, how he recruited
18 patients or how he recruited investigators to the study. On slide 66, he talks
19 about how he's listed on the first page of the Bouabdallaoui paper and how
20 he's the primary author of the paper, but not necessarily the sole author. He
21 also talked about how he provided information about COLCOT study results
22 to Bouabdallaoui.

23 On slide 69, he talks about the Bouabdallaoui reference, which is a
24 publication of my invention, or substantively the same subject matter of my
25 invention. On slide 70, this is the first time that during deposition when we
26 asked him if he's the sole inventor and if he came up with the time period

1 limitations, he said yes, but there's no corroboration. There is no review of
2 the patent to look at the claims to make sure that he truly is the sole inventor
3 and nobody else.

4 When we look at Dr. Ardehali's declaration, he just provided an
5 opinion, but he has no personal knowledge. So Dr. Ardehali is probably not
6 qualified to talk about who the inventor here is.

7 On slide 72, Dr. Bouabdallaoui's declaration, she says she does not
8 consider herself an inventor. Well, what does that mean? It's unknown. So
9 what we've received is just a lot of things that quite frankly don't matter
10 when it comes to an inventorship analysis. Who conceived and designed of
11 COLCOT? Who recruited investigators? Who got the funding? None of
12 that matters.

13 What matters is facts and corroboration in the form of facts,
14 documents, emails, anything like that to corroborate that Dr. Tardif is in fact
15 the sole inventor. And again, it does not matter who came up with
16 COLCOT. We are not disputing COLCOT. We're talking about the specific
17 0-3 day time limitation. And that's what we don't have information about.
18 There's no corroboration. So where's the corroboration?

19 Slide 74. MHI has had the burden ever since trial institution to
20 come up with corroborating evidence. And they haven't done that. The
21 evidence is in their possession, but they don't have it. At best, we have two
22 false statements from Dr. Tardif's deposition, but no corroborating evidence
23 to back it up.

24 And if you remember, Dr. Bouabdallaoui, we had to fight for her
25 deposition. And what we learned in her deposition were about these
26 brainstorming sessions. She was part of the brainstorming, Dr. Tardif was

1 part of the brainstorming, and so were others from the group.

2 And she does not remember who came up with the 0-3 day, but she
3 did say in her deposition that it's not a one-person idea, that these were
4 brainstorming sessions where Dr. Tardif suggested to the group that they
5 look at the COLCOT database and come up with new ideas of what to
6 investigate based on it.

7 So even after learning of the brainstorming sessions, this is on slide
8 76, we got no further details about those brainstorming sessions from Dr.
9 Tardif or any sort of clarifications about those brainstorming sessions. We
10 certainly haven't received any notes from them, no emails, no
11 contemporaneous documents, no testimony from any others about these
12 brainstorming sessions except from Dr. Bouabdallaoui.

13 So, you know, we don't know who came up with this 0-3 day time
14 period because we don't have that information. But Patent Owner most
15 certainly does have that information, and they haven't shared it. So here are
16 some slides starting at page -- or slide 77 that just goes through the
17 deposition of Dr. Bouabdallaoui where she says that it's not a one-person
18 idea.

19 So on slide 80, if you look at the evidence kind of from both sides
20 here, on the one side we have absolutely zero evidence corroborating that
21 Dr. Tardif is the sole inventor of the 0-3 day TTI. But on the other side we
22 do have a lot of evidence, maybe circumstantial, maybe not, but a lot of
23 evidence to show that somebody at least also participated in conceiving of
24 this 0-3 day time period limitation.

25 It may be Dr. Bouabdallaoui, because she certainly has experience
26 doing time-based post hoc analyses. She's the one who interpreted the

1 results and she wrote the manuscript. Or it might be somebody else. We
2 don't know. But what we do know seems to show that it's not just Dr.
3 Tardif.

4 Right now I would like to turn to slide 84. Patent Owner is trying
5 to argue that these brainstorming sessions were directed to other post hoc
6 analyses. But if we go back to some of the slides quoted here, you'll see that
7 Dr. Bouabdallaoui talked about brainstorming sessions in general and how
8 this applied to all brainstorming sessions, not just the ones, or that this
9 applied to brainstorming sessions that gave rise to this particular 0-3 day
10 time limitation.

11 Dr. Tardif never mentioned brainstorming sessions. So for Patent
12 Owner to say that both witnesses were clear that additional brainstorming
13 sessions addressed other post hoc analyses is just plain wrong.

14 Patent Owner also tries to argue that Bouabdallaoui disavowed her
15 inventorship. I have no clue what that means. Under U.S. patent law, you
16 cannot disavow your inventorship. It's a legal determination. Either you are
17 an inventor because you conceived of the claim limitation, or you're not. So
18 it's a very factual and legal determination. So the facts, not anybody's
19 wishes, control who is an inventor.

20 Patent Owner now wishes to also say that this argument is moot
21 because they can correct inventorship if they need be, but this is a new
22 argument and Patent Owner has not sought permission to correct
23 inventorship and it should also not be granted at this late stage of the game.

24 And as just a final slide to leave you with, nobody has ever
25 actually confirmed that Dr. Tardif is the sole inventor, not even Patent
26 Owner. Even in the latest opposition to the motion to exclude, nobody -- the

1 attorneys have not even said that Dr. Tardif is the sole inventor. Every
2 sentence they say is a bit of a hedging on the issue.

3 And MHI's expert also has a misunderstanding of the inventorship
4 analyses. And if you read his deposition, he believes that inventorship
5 should be handed out as a reward for doing work in his lab. And at this
6 point, Patent Owner is just hedging to say that they can correct inventorship.
7 So without ever showing any sort of evidence to corroborate Dr. Tardif's
8 sole inventorship claim, now they're saying that they can fix it if they need
9 to. This is nothing more than just hedging. I'm glad to take any questions.

10 JUDGE JENKS: I do not have any questions at this time. I
11 believe your allotted time is up.

12 MS. BROUGHER: Thank you.

13 JUDGE JENKS: Instead of taking a break now, we will hear from
14 Patent Owner and then take a break after Patent Owner's initial arguments.

15 MR. PATEL: Thank you, Your Honor.

16 JUDGE JENKS: Before you begin, can I ask you if you would
17 like to reserve some time for surrebuttal?

18 MR. PATEL: Yes, we'd like to reserve 10 minutes for surrebuttal.

19 JUDGE JENKS: Just to give you a warning, we might have to
20 take our break somewhere at, what is it, it would be 2:20. Would that be
21 okay for you?

22 MR. PATEL: That should be fine, yeah. That would be actually a
23 good stopping point probably for me to turn it over to my colleague.

24 JUDGE JENKS: Excellent. And we'll take a stop at that point or
25 time. Thank you so much.

26 MR. PATEL: Thank you. May it please the Board. If we can turn

1 to slide 2, it provides an outline of what we're going to be arguing today. I
2 will be discussing the background of the relevant art, provide some
3 background on the '063 Patent, and Dr. Tardif's surprising discovery. And
4 then I will also address claim construction, the issues of claim construction.
5 And then the specific grounds themselves will be handled by my colleague,
6 Mr. Wilkerson.

7 So before delving into the claims, I want to talk about the relevant
8 field in this case. The relevant field here is medicine and particularly
9 preventive medicine. Now, the medical field is highly unpredictable. It's
10 probably one of the most unpredictable of fields because, unlike bench
11 chemistry which I did many years ago, medical research requires large
12 clinical trials with hundreds or thousands of patients in various locations.

13 The field of the '063 Patent is even more unpredictable than the
14 typical method of treatment claims because the claims are directed to
15 preventative treatment. They are directed to the methods of reducing the
16 risk of stroke and other conditions after myocardial infarction. As a result,
17 the claims are not focused on short-term effects on a patient, but attempts to
18 predict future effects. In other words, these studies are looking at long-term
19 outcomes.

20 To invalidate the claims, Petitioner must demonstrate that a POSA
21 would be able to predict with a reasonable expectation of success and
22 without undue experimentation that, one, there would be a reduced risk of
23 certain events, including stroke -- reduced risk of certain cardiovascular
24 events, including stroke, in the future. Two, that it be safe and tolerable.
25 And three, that it not cause or increase the risk of other side effects or
26 diseases.

1 In preventative medicine, all of these factors must be taken into
2 account. It's not just efficacy. As we'll show, a POSA at the time of the
3 invention would not be able to predict with a reasonable expectation of
4 success and without performing undue experimentation that initiating this
5 low dose of colchicine very soon after an MI when a patient may or may not
6 be stable would reduce the risk of stroke and other claimed cardiovascular
7 conditions.

8 So now if we turn to the next slide, slide 3, I believe Petitioner
9 already talked about the Colcrys product. As Petitioner mentioned, that was
10 directed to gout and familial Mediterranean fever, which are both very
11 different from cardiovascular conditions.

12 Beginning in the early 1990s, clinical studies using colchicine in
13 the cardiovascular setting were first performed. And as I'll describe, many
14 of them found that colchicine, sometimes even at the same dose as the
15 claims and similar timeframes, did not have an effect or at best were
16 inconclusive.

17 So let's go to slide 4. This is Exhibit 2009. This is the O'Keefe
18 article from 1992. And this was an animal study where colchicine was
19 tested on rabbits. It was administered at the time of a coronary angioplasty,
20 but it was found not to have any effect on the rate of restenosis. And
21 restenosis is basically a cardiovascular condition where there is a reduction
22 in the diameter of the blood vessels.

23 So Exhibit 2009 would have indicated to a POSA that colchicine
24 was only found to have an effect at dangerously high dosages in animal
25 models, while a relatively safe dosage of 1.2 milligrams per day was not
26 effective.

1 Now turning to slide 5, two additional prior art studies would have
2 dissuaded a POSA from the use of low-dose colchicine to reduce the risk of
3 cardiovascular diseases. The first here is Raju 2012. It's a study from 2012.
4 It's Exhibit 2054, and it's a pilot study where colchicine was initiated after
5 admission to hospital with an acute atherothrombotic vascular event, and the
6 study provided no evidence that colchicine, compared with placebo,
7 suppressed the high sensitive C-reactive protein.

8 And the high sensitive C-reactive protein is basically an
9 inflammatory triggering protein, and it's one of the key indicators of
10 potential recurrence of cardiovascular disease.

11 Next, we have Exhibit 1028, which is the Hennessy 2019 article
12 that Petitioner discussed. This is a LoDoCo MI trial. Now, this discloses an
13 investigator-initiated randomized placebo-controlled trial. In this study, 0.5
14 milligrams of colchicine was administered once daily, which is the same
15 dose as the patent, and it was administered to adults who had recently
16 sustained an acute myocardial infarction within the prior seven days.

17 So this study, the conclusion from the study, as you can see here,
18 was that low-dose colchicine was not effective and was not able to
19 sufficiently lower the CRP levels. This study would tend to lead a POSA
20 away from colchicine and perhaps try something else. It did not show
21 efficacy.

22 Next, we also have -- Exhibit 1028 also later says that the totality
23 of the evidence supports the need for a large-scale outcome study. Sorry, the
24 HDMI plug was a little loose there. So as I mentioned, the Exhibit 1028 also
25 suggested to do a large-scale outcome study, and this was done by Dr. Tardif
26 in COLCOT, and he was able to show that colchicine is effective when it is

1 administered very early.

2 Another prior art study at 2055, Exhibit 2055, is the Akodad study
3 in January 2017. This is known as the COLIN clinical trial, and it tested the
4 treatment of colchicine in patients with acute myocardial infarction and
5 inflammatory response. Now, this study was also inconclusive with respect
6 to the effect of colchicine. It says it right there in the blowout. And it found
7 no improvement in inflammatory profiles or the diminution of the infarct
8 size.

9 So now, CRP, as I mentioned, is very relevant to whether or not
10 subsequent cardiovascular events occur. Dr. Ridker, the plaintiff's expert,
11 has spent a lot of time and research papers looking at the link between CRP
12 and subsequent cardiovascular events. Now, this is the '063 Patent, of
13 course, in this case, with a priority date of November 15, 2019. And Dr.
14 Tardif's novel treatment method is reflected in the claims.

15 And Dr. Tardif did several things that were not typical. He did
16 several things that just were not typical in the art, and this further increases
17 the unpredictability of whether or not the treatment would be safe and
18 effective.

19 So, turning to slide 8, are the independent claims 1 and 8. As you
20 can see in these claims, Dr. Tardif went against the grain and conventional
21 wisdom and administered colchicine very soon, within about three days after
22 an MI, whereas the conventional wisdom was to wait until the patient had
23 stabilized. You'll see when Mr. Wilkerson argues that LoDoCo and these
24 other studies waited almost six months after stabilization for the patient to
25 start treatment.

26 So, in hindsight, it's easy to say that colchicine is an old drug, and

1 so it would be obvious to not have any adverse effects. But in the medical
2 field, until it's tested on a specific cohort, a POSA would not know how it
3 would affect that specific patient population. And here, it's a unique cohort
4 of very sick patients who had suffered an MI within the last three days, and
5 they may or may not be stable in that period of time. It depends on the
6 patient.

7 And the prior uses, as Petitioner mentioned, gout and familial
8 Mediterranean fever, would not have provided sufficient information to a
9 POSA on the effect colchicine would have on a patient who recently
10 suffered an MI.

11 Now, second, Dr. Tardif went against conventional wisdom
12 because he initiated treatment without using a higher loading dose. As Dr.
13 Ardehali and others testified, it was conventional wisdom or practice. It was
14 a standard of care to use a loading dose before starting a low-dose colchicine
15 therapy. Instead, Dr. Tardif skipped the loading dose and started right from
16 the outset with low dose.

17 Now, I'd like to -- we have Claim 27 in slide 9, which is the third
18 independent claim in this case. And it's directed to the novel finding that
19 this method reduced the risk of stroke. As I mentioned earlier, we looked at
20 the LoDoCo and other studies, and they were inconclusive.

21 And before I turn to the issue of claim construction, I'd briefly like
22 to address inventorship, which is that issue with respect to this patent. And
23 as I mentioned, when research is conducted in a large clinical setting, the
24 principal investigator will work with a team of professionals. This includes
25 statisticians. And that's what Dr. Tardif did here. It's indisputable that he
26 was the principal investigator.

1 Petitioner simply speculates that Dr. Bouabdallaoui may be an
2 inventor because she appears first on a paper where Dr. Tardif is the
3 corresponding author. And it's known that the corresponding author is
4 responsible for the contents of the paper. And nobody disputes that in this
5 case.

6 Also, in response to the allegation, Patent Owner provided a
7 declaration from Dr. Tardif explicitly stating that it was his invention and
8 providing a reasonable explanation as to why there were other authors listed
9 there and why Dr. Bouabdallaoui was listed first. This is called a Katz
10 declaration, and it's under MPEP 2155.01.

11 Not only that, then Patent Owner corroborated his testimony with a
12 declaration from Dr. Bouabdallaoui, who explained that she was, and
13 everybody else, was working under the direction of Dr. Tardif. Now,
14 Petitioner has shown isolated excerpts of deposition testimony. But they just
15 simply do not comport with the totality of the evidence in this case, as Mr.
16 Wilkerson will discuss. It's all speculation and wishful thinking that Dr.
17 Bouabdallaoui is an inventor. They --

18 JUDGE JENKS: Can I -- I'm sorry.

19 MR. PATEL: Yes, Your Honor.

20 JUDGE JENKS: Can I interrupt you for a second? I mean, I
21 obviously have to struggle. You know, Katzdeclarations are often used in
22 prosecution when they're presented to the examiner. And an examiner, in
23 essence, takes the Katz declaration at face value. They're told to take it at
24 face value because there isn't an opportunity to question witnesses and get
25 more information. So here in our AIA proceedings, we do have the ability
26 to question the witnesses and get a little bit more information.

1 So it would seem to me that maybe you need to do a little more
2 than just provide what in essence becomes the Katz declaration. And you
3 had the opportunity to provide us with research agreements for these various
4 institutions, letting us know that really they're just being the pawns in this
5 particular study. And that might persuade us to the point where that maybe
6 Dr. Tardif is the sole person responsible for this article. So do you see that
7 there's a difference between --

8 MR. PATEL: No, absolutely. I understand the difference.

9 JUDGE JENKS: -- what's happening here -- and going --on in
10 prosecution.

11 MR. PATEL: Yes, I understand the difference. And here there
12 was additional discovery provided, as you know, Your Honor. There were
13 depositions of both Dr. Bouabdallaoui and Dr. Tardif. And their testimony
14 overall will demonstrate that Dr. Tardif is the sole inventor. Dr.
15 Bouabdallaoui clearly testified that she was not. They worked with a patent
16 attorney.

17 And there's a very simple explanation as to why Dr. Bouabdallaoui
18 was listed first. Yes, she did write the first draft of the manuscript. But both
19 Dr. Tardif and Dr. Bouabdallaoui were clear that she was listed as a first
20 named author because she helped and she was a young investigator, not
21 because she made an inventive contribution.

22 Now, Petitioner goes so far as to rely on boilerplate language from
23 the USPTO's Declaration of Inventorship form where Dr. Tardif simply
24 ticked the box that said either I am the sole or the joint inventor. This alone
25 indicates that Petitioner has very little evidence to support their joint
26 inventorship allegation.

1 Now, Petitioner also says that Patent Owner didn't produce other
2 documents supporting Dr. Tardif's sole inventorship. Well, it was
3 Petitioner's idea to bring this action in the PTAB. They knew full well the
4 amount of discovery that's afforded in this forum. They could have brought
5 this action and filed a declaratory judgment action in the district court and
6 have obtained all sorts of written discovery. They had not asked for written
7 discovery.

8 And we did provide them plenty of time to ask Dr. Tardif and Dr.
9 Bouabdallaoui all of the questions that they needed to regarding notes or
10 conception or reduction to practice. They had the time to do that. So,
11 respectfully, we assert that Patent Owner has met its burden to demonstrate
12 that Dr. Tardif is the sole inventor, and we have provided corroboration from
13 Dr. Bouabdallaoui, and we should not be penalized for Petitioner's decision
14 to bring an action here in the IPR and not in a different forum.

15 Now, I'd like to turn to the issue of claim construction, unless there
16 are any other questions.

17 JUDGE JENKS: I don't have any other questions.

18 JUDGE SNEDDEN: If you can clarify your corroborating
19 evidence is the testimony of Dr. Bouabdallaoui.

20 MR. PATEL: Yes, it's her testimony. It's her declaration. Those
21 are corroborating evidence as well as Dr. Tardif's own declaration where he
22 declared that he is an inventor of the patent. And nobody else filed a
23 declaration of inventorship. So that demonstrates that he was the only
24 inventor.

25 JUDGE YANG: So about this exhibit, there are more than two
26 authors, right? There are more than a dozen, a truly national collaboration.

1 So all the other people, what's their role?

2 MR. PATEL: Yeah, they were all clinical investigators working
3 under the direction and supervision of Dr. Tardif. So these individuals may
4 be running the trial at different sites. And so when they had these meetings,
5 these meetings were run by Dr. Tardif. And everybody was working under
6 his supervision. That's typically the case in a clinical trial. The principal
7 investigator needs to work with a lot of different individuals, unlike other
8 types of research.

9 And so these other individuals were working under his direction
10 and supervision. They may have participated in those meetings, but they did
11 not have an inventive contribution. Some of them were like statisticians, for
12 example, and others played other roles.

13 JUDGE YANG: I hear you. So this is just based on Dr. Tardif's
14 declaration or testimony. Do we have any other evidence to --

15 MR. PATEL: Yes, we have Dr. Bouabdallaoui's.

16 JUDGE YANG: Just to say all the other authors didn't contribute.

17 MR. PATEL: Exactly. I mean, she testifies several times in her
18 deposition that in these brainstorming sessions, Dr. Tardif led those sessions
19 and that everyone was working under his direction and supervision. So they
20 may have participated in the meetings, but there's no evidence that they
21 contributed any inventive -- that they made any inventive contribution to this
22 patent.

23 If anything, all of the evidence in this case demonstrates the
24 opposite. There's testimony from both Dr. Tardif and Dr. Bouabdallaoui that
25 is consistent and corroborates each other with respect to inventorship.

26 JUDGE SNEDDEN: Do we have any affirmative statements from

1 Dr. Bouabdallaoui that it was Dr. Tardif that came up with these?

2 MR. PATEL: Yes, we do. And if we can turn to -- yeah, it's at
3 page 64, line 9 to 22. Right here. And this is from Dr. Bouabdallaoui's
4 deposition, page 64, line 22, where she states that in these brainstorming
5 sessions, Dr. Tardif led the discussions and she was part of the team and
6 working with him at the time. She was one of his students at the time.

7 JUDGE YANG: Counsel for Petitioner earlier points out we are
8 not talking about a general idea. We're talking about the 0-3 days and the 4-
9 7 days etc.

10 MR. PATEL: Yes.

11 JUDGE YANG: So you are saying during all these brainstorming
12 sessions, all these ideas came from Dr. Tardif and he directed the others?

13 MR. PATEL: Yes, and Dr. Tardif testifies to that effect, and so
14 does Dr. Bouabdallaoui. But she didn't remember exactly who came up with
15 the 0-3 days, because those meetings were many years ago. And at the end
16 of the day, basically we can't prove a negative. We can't prove that nobody
17 else contributed to the patent. The evidence that we do have shows that Dr.
18 Tardif is the sole inventor. Any other questions before I move to claim
19 construction?

20 JUDGE JENKS: I do. Can we go back just one step here?

21 MR. PATEL: Sure.

22 JUDGE JENKS: I mean, I'm just puzzled that we have this
23 reference, the 105 --

24 MR. PATEL: Yeah, 1005.

25 JUDGE JENKS: 1005, that particular reference. It has I think
26 something like 19 institutions participating in it, and you did provide some

1 clinical trial agreements as evidence. However, I went through it and I
2 found only one of the exhibits that you provided is actually also associated
3 with one of the universities, one of the institutions that would be Exhibit
4 2012.

5 But you didn't provide us with the same types of agreements
6 between all these other institutions, which might be persuasive evidence to
7 say that they're just participating as puppets in this particular study. And
8 three of them you provided aren't even listed as institutions in this particular
9 paper and participated. So is there a reason we didn't get the others?

10 MR. PATEL: I think we did. There's no reason that I'm aware of
11 as to why those other documents were not produced. I think there were, you
12 know, and actually I would turn -- that question is probably better for Mr.
13 Wilkerson because he was dealing with the document production in this
14 case. But we did provide several documents to show that these other
15 institutions were essentially working as pawns for Dr. Tardif.

16 Moreover, as Mr. Wilkerson will discuss, there's other reasons why
17 the Bouabdallaoui reference is not prior art, and that's based on the priority
18 date, which Mr. Wilkerson will discuss.

19 JUDGE JENKS: Okay.

20 MR. PATEL: So if we go to claim construction. So I'd like to turn
21 to the preamble, which is in Claim 27. So let's start with the legal standard
22 here and the relevant cases for construction of the preamble. As we know,
23 the preamble is limiting if it breathes life meaning or vitality into the claim.

24 And in the Boehringer Ingelheim case, the Federal Circuit had also
25 distinguished method claims from other types of claims, stating that, as it
26 frequently does for method claims, preambles are not merely the

1 circumstance in which the method may be useful, but instead are the raison
2 d'être of the claimed method itself. Also, relevant law is when a preamble
3 provides antecedent basis to other elements in the claim. It's an indication
4 that the preamble should be limiting.

5 Finally, the Federal Circuit has made clear that when a preamble is
6 relied upon to distinguish the claim over the prior art, that transforms the
7 preamble into a material limitation. And we'll show that that's what
8 happened here. The preamble is a method of reducing the risk of stroke.

9 Now, Claim 27's preamble satisfies all the tests provided by the
10 Federal Circuit for material limitation. First, it does breathe life meaning
11 into the claim. Without it, the rest of the claim is an academic exercise. It
12 provides the purpose of the administration. We respectfully disagree that it
13 simply identifies the population --

14 JUDGE JENKS: I'm sorry, I do have a question for you on this
15 one. We have a method of reducing the risk of stroke in a patient having
16 MI, myocardial infarction. How do I know which of my patients that have
17 myocardial infarction are at a risk of stroke versus those that are not? I
18 mean, these would then be two different patient populations, right? You're
19 saying not every -- you know, you're trying to breathe life into this, but that
20 would indicate that not everybody who has an MI is at risk of stroke, and so
21 therefore we can reduce it.

22 Here we're just saying, you know, take a patient with an MI, give
23 them this medicine, and you know what? It's the same patient population.
24 They will also have a reduced risk of stroke. What I don't have is how can I
25 distinguish which patients to give medicine to so I can reduce the risk of
26 stroke.

1 MR. PATEL: Well, it is patients who have had an MI, you know,
2 within the last 30 days.

3 JUDGE JENKS: Yeah, that's my patient population. That's what
4 the, what's it called, is it the COLCOT study, which is what it's saying?

5 MR. PATEL: Yes.

6 JUDGE JENKS: Give it to this population within 30 days.

7 MR. PATEL: That's --

8 JUDGE JENKS: Why would it not just reduce the risk of stroke in
9 those patients?

10 MR. PATEL: It's not necessarily going to reduce the stroke in
11 every patient. You know, overall, the cohort, there might be a reduction of
12 stroke, but not every patient is going to have a reduced risk. So there are
13 some patients for whom it may not be reduced.

14 JUDGE JENKS: But I'm still giving it to them, the people who
15 have MI. And some will have a reduced risk of stroke or will not have a
16 reduced risk of stroke versus others don't. I just can't -- what I'm having a
17 problem with is how can I look at my patient and say I'm going to give
18 medicine to you because I want you to prevent stroke in the long run, and I
19 can somehow tell that this is going to affect you better than my other my
20 other MI patients.

21 Do you understand this? That's kind of what we would need to sit
22 there and say, here we have COLCOT tells us take MI patients within 30
23 days, give them colchicine. And my question is why wouldn't that also
24 reduce the risk of stroke?

25 MR. PATEL: It's not going to necessarily result in the reduction of
26 stroke. And all patients -- so we talked about the antecedent basis. Also, the

1 reliance by the examiner and -- importantly the reliance by the examiner in
2 the notice of allowance of the preamble converts it into a material limitation.
3 It was required for patentability. The intrinsic evidence also -- the
4 specification also talks about the reduction of stroke. So it is essentially the
5 purpose for the client.

6 JUDGE SNEDDEN: Okay. I have a question.

7 MR. PATEL: Uh-huh.

8 JUDGE SNEDDEN: Assuming we agree with you that the
9 preamble is limiting, when I read the Exhibit 1006, the COLCOT protocol,
10 I'm having trouble finding any distinguishing features between -- what's the
11 difference between the protocol and what's in the claim? Because here,
12 when I read the protocol, it mentions that it evaluates whether long-term
13 treatment reduces the rates of cardiovascular events.

14 MR. PATEL: Yes.

15 JUDGE SNEDDEN: One of which is a stroke.

16 MR. PATEL: Yeah, but the surprising discovery was the specific
17 reduction in the risk of stroke. That's the distinction, that's the novel
18 discovery that Dr. Tardif made after doing this post hoc analysis.

19 JUDGE SNEDDEN: Okay. So he showed that it worked?

20 MR. PATEL: He showed that it actually had a pronounced
21 decrease in the risk of stroke after doing that post hoc analysis. And the data
22 shows that it was a very significant reduction. I don't know off the top of
23 my head exactly what it was, Mr. Wilkerson probably knows better. But it
24 was a significant reduction.

25 JUDGE SNEDDEN: And let me understand, that information
26 would appear to help you if this was an obviousness ground, but it's an

1 anticipation ground.

2 MR. PATEL: Let me address that. There's no direct disclosure of
3 that reduction of stroke in COCLOT. So it can't anticipate either.

4 JUDGE SNEDDEN: I see. So basically your position is that the
5 COCLOT protocol does not teach the preamble of Claim 27.

6 MR. PATEL: That's right.

7 JUDGE SNEDDEN: Okay.

8 MR. PATEL: And so that preamble has to be limited, and that's
9 what the examiner relied on as well in allowing the claim. He stated that in
10 his reason of allowance, that the prior art did not teach that, the reduction of
11 stroke, explicitly.

12 JUDGE SNEDDEN: Okay, understood. Thank you.

13 MR. PATEL: Thank you. So I want to talk about the law that
14 Petitioner decided, and that's frankly in apposite to the claims at issue here.
15 So, for example, the Bristol-Myers BMS case is distinguishable because --
16 and in that case the preamble was for reducing hematologic activity. The
17 court found that it was not limiting, because it was not required for
18 patentability.

19 The court explicitly said that it was not a new use of a process that
20 was relied upon to distinguish the process from the prior art. Whereas here,
21 we are talking about the discovery that reduced the risk of stroke after an
22 MI, that's a new use, and that distinguishes Claim 27 from the prior art. And
23 here, the method is also novel compared to what was in BMS, where the
24 method was the same as the prior art.

25 Now, Petitioner has made some comments about manipulative
26 difference, but the manipulative difference is not the standard. It's an

1 indicator, but it's not the standard. The standard is whether or not the
2 preamble breathes life meaning and vitality into the claim. And certainly
3 that's what this preamble does with respect to this claim. Without it, it's just
4 an academic exercise.

5 I mean, you could administer this for treating, preventing, causing.
6 You could administer the colchicine for any disease, any condition: gout,
7 FMF. It just becomes an academic exercise without the preamble.

8 Now, the other cases, IMS Tech and Rowe v. Dror are
9 distinguishable because they don't even deal with method claims. They deal
10 with an apparatus claims, which is very different, a different field from the
11 field of medicine, and different types of claims. In IMS Tech, the preamble
12 was a control apparatus, and it was found not to be limiting because it didn't
13 add a limitation to the body of the claim. The apparatus was able to stand on
14 its own without the preamble.

15 So let's move to the Claim 8, which are the wherein clauses. And
16 just to address the relevant law here, which is the Allergan case, and that
17 case is the closest case to this situation here. And it states that where a
18 condition is material to patentability, it cannot be ignored to change the
19 substance of the invention. And here it's clear that these wherein clauses
20 were material to patentability, and they also provide antecedent basis.

21 So let's look at Claim 8, and the wherein clauses here are
22 highlighted in yellow. This claim actually has three wherein clauses, but the
23 ones that were at issue are the last two. And the Circuit two wherein clauses
24 relate to the lowered risk of certain cardiovascular events with colchicine
25 compared to without colchicine.

26 Now, if we look at this slide, this is a comparison of the claims,

1 Claim 8 and the claim in Allergan. So both cases are in the same field,
2 they're in the medical field. Both relate to method of treating a patient that
3 results in some improvement over the prior art. And the wherein clause in
4 Claim 8 and the wherein clauses in Allergan are both directed to the result of
5 the claimed method compared to other methods of treatment.

6 And the Federal Circuit found in Allergan that these wherein
7 clauses were material limitations that could not be ignored. Now, moreover,
8 in Allergan, these were found to be a material limitation despite not
9 providing antecedent basis. Here, the wherein clauses do provide antecedent
10 basis to some of the terms.

11 Now, if we look at the next slide, this slide finally shows that the
12 wherein clauses were material to patentability. Here's another notice of
13 allowance, another section of it. The examiner specifically says that the
14 reference prior art does not suggest or make obvious the cardiovascular
15 events, including stroke.

16 So these wherein clauses and the preamble are limiting because
17 they're material to patentability. They provide antecedent basis, and the
18 preamble brings life and meaning into the claim, without which the claim is
19 just an academic exercise. So with this, I'll turn it over to my colleague, Mr.
20 Wilkerson, unless there are any questions or we want to take a break.

21 JUDGE JENKS: I think we're going to take a break at this point in
22 time and then have Mr. Wilkerson continue. So we will take a ten-minute
23 break. Is that enough?

24 MR. PATEL: Yes.

25 (Whereupon, the above-entitled matter went off the record at 2:27
26 p.m. and resumed at 2:39 p.m.)

1 JUDGE JENKS: All right. Mr. Wilkerson?

2 MR. WILKERSON: Yes, Your Honor.

3 JUDGE JENKS: You may begin when ready.

4 MR. WILKERSON: Good afternoon, and may it please the Board.

5 My name is Matthew Wilkerson on behalf of the patent owner. As my
6 colleague, Mr. Patel explained, today I'll be covering Petitioners Grounds 1-
7 4. To orient ourselves a little bit, I do want to let you all know that I'll begin
8 with Grounds 1 and 4, which both concern Exhibit 1005 as a key prior art
9 reference, and then we'll proceed to Grounds 2 and 3 which, as Your Honors
10 may recall, involves the COLCOT Protocol Summary, Exhibit 1006 as a key
11 prior art reference.

12 Directing you to Slide 24, Your Honors, and here's just a summary
13 of the primary basis of why the Bouabdallaoui reference is not prior art. I
14 really want to focus on the priority date issue, given Mr. Patel's discussions
15 with you all on the inventorship. However, I do want to flag one issue with
16 the inventorship before we proceed, and that's to make clear for the Board
17 that there is no hedging at all on the part of Patent Owner. Patent Owner
18 affirmatively and consistently has asserted that Dr. Tardif is the sole
19 inventor.

20 I know you heard some argument from opposing counsel that
21 maybe put that into question, but in Paper 21, the patent owner's response at
22 page 17, the first full paragraph opens, as Patent Owner explained in its
23 preliminary response, Dr. Tardif, the sole inventor of the '063 Patent, is also
24 the lead author of Bouabdallaoui, and that has not ever changed in our
25 positions or our arguments.

26 Moving on to the priority date issue here at Slide 25, some facts

1 are undisputed. Firstly, it's undisputed that the provisional application, the
2 865, was filed on November 15, 2019. It's also undisputed that the earliest
3 publication date for the Bouabdallaoui reference, Exhibit 1005, is August 29,
4 2020, ten months after that first provisional was filed.

5 Really importantly, that first provisional application, the 865, filed
6 in November of 2019, disclosed the time to initiate limitations that are found
7 in the '063 Patent. Opposing counsel argued that nowhere does it say 3 days,
8 nowhere does it say 4-7. However, very importantly, in the file history and
9 in that provisional application specification, the inventor disclosed
10 embodiments where involving administering colchicine within 5 days of the
11 MI.

12 As Your Honors may recall, in the institution decision, there was
13 some claim construction around the term within about 3 days as compared to
14 the term in the provisional of within 5 days. And Your Honors found that
15 within about 3 days encompasses days 1, 2, and 3. Alternatively, absent the
16 about, within 5 days encompasses days 1, 2, 3, and 4.

17 So what we see here is a provisional application, both in the
18 specification and if you see on the next slide 26, explicitly claimed is that
19 days 1, 2, 3, and 4. It is entirely within the realm of common practice in
20 patent prosecution for a claim to be modified or amended after the non-
21 provisional is filed, let alone after the provisional. And here we have a
22 circumstance where that first provisional filing encompassed entirely the
23 claimed time to initiate treatment limitations.

24 And in fact, under the Board's interpretation, reduced that window
25 for these Claims 1 and 8 by a mere one day. Similarly, the time to initiate
26 treatment recited in Claim 28, which goes within 4-7 days, was disclosed

1 with even a narrower claim of administering within 10 days of the MI.

2 This is not a circumstance in which the inventor put a general
3 initiate colchicine claim down and then thereafter in the non-provisional
4 selected days. Now, the evidence is clear that Dr. Tardif recognized his
5 invention of time to initiate treatment early on, and he held his place in line
6 with that priority date with the submission of the 865 provisional
7 application.

8 Importantly, even though we've heard a lot today about
9 inventorship, as far as Grounds 1 and 4 go, the Board may stop there,
10 regardless of the correct inventorship. Regardless of who is the correct lead
11 author of Exhibit 1005. Based alone on the priority date, it is not prior art,
12 and therefore not an invalidating reference.

13 Other evidence corroborates that priority date. In fact, Petitioner's
14 own expert, Dr. Ridker, did not find any criticality within the difference of a
15 3 day window and a 5 day window. He opined in his declaration that they're
16 different. They don't overlap. They're not the same. Yet when questioned
17 at deposition, he could not explain why.

18 Instead, Dr. Ridker consistently testified that in his opinion, the
19 importance is placed on the stability of the patient, not the date at which it is
20 initiated. So their own expert places no criticality on this claim limitation
21 that they say is not entitled to the earliest priority date.

22 Additionally, the Bouabdallaoui reference was before the
23 examiner, after this time, and the examiner did not consider that reference in
24 its prior art determinations, did not consider that reference in any of its
25 rejections. And finally, the Bouabdallaoui reference itself, in the
26 disclosures, Dr. Tardif discloses his pending application, which at the time

1 was the 865 provisional application. He could not have disclosed that as a
2 conflict of interest if it did not contain the same subject matter he was
3 publishing in this paper.

4 However, even if the Board finds that there is not proper earlier
5 priority date, this was still published within the one year grace period of the
6 latest possible priority date. There's no dispute about that latest possible
7 priority date. The dispute lies in two things. The first is who is the true
8 author of the Bouabdallaoui reference. The second is inventorship.

9 Originally in the petition, and before institution, Petitioner only said Dr.
10 Tardif is not the author. There was no argument on inventorship, just merely
11 that Dr. Tardif was not the author of Bouabdallaoui.

12 In response, Patent Owner provided several pieces of information
13 that showed Dr. Tardif is the inventor. Dr. Tardif is the elite author. He's
14 the only corresponding author. They haven't disputed he's the only
15 corresponding author. They just say that a POSA would disregard that.
16 That's not true.

17 Under AIA 102(b), if the Board finds the latest possible priority
18 date for the '063 Patent, the Bouabdallaoui reference represents a publication
19 made within one year by the inventor or by another, even if there's another,
20 if we're saying all the other authors are included, by others who obtain the
21 subject matter directly or indirectly from the inventor, Dr. Tardif.

22 And unless Your Honors have more in-depth questions on
23 inventorship, I just want to touch on a few points. Counsel says that they're
24 confused about what it means to disavow inventorship. Frankly, Patent
25 Owner I believe it's very simple. We have a really unique situation here and
26 one that none of Petitioner's case law applies to, including the frame-shifting

1 of Drinkwater -- the burden-shifting of Drinkware, excuse me.

2 Here, Petitioner is demanding that someone who says I'm not an
3 inventor is an inventor. All the other cases they rely on involves instances in
4 which someone who tries to raise their hand and say, I am an inventor, I've
5 been unfairly excluded, or my rights have been unfairly withheld for me
6 because I am an inventor. It's the opposite here. The person that Petitioner
7 points to and says, this person must be an inventor and we're somehow
8 hiding the ball, is saying, wait, I'm not an inventor. I'm not involved. This
9 is not me. I did not come up with this.

10 So the whole idea of a burden shifting and there being a burden of
11 proof or production on Patent Owner here just doesn't apply. As Mr. Patel
12 pointed out, there's a forcing of proving a negative. It's almost as if we're
13 being forced to prove that Dr. Bouabdallaoui is not the inventor. Well, that's
14 not the standard. It's not the standard.

15 And even if there is a burden of production upon Patent Owner, as
16 Your Honor's already correctly pointed out, we provided the declaration of
17 Dr. Tardif, along with exhibits disclosing the agreements for the COLCOT
18 trial, which became the Bouabdallaoui reference and then became the same
19 thing that is claimed in the '063 Patent.

20 So we're all talking about the same thing here, and we talk about
21 the COLCOT study itself. Not Exhibit 1006, the summary of the protocol
22 on ClinicalTrials.gov, that describes what was executed through all this hard
23 work by Dr. Tardif and his colleagues. And so that's why Dr. Tardif, as
24 we've consistently said, is the sole inventor of the '063 Patent. That's why
25 the Bouabdallaoui reference is his work and no one else. And that's why the
26 '063 Patent is entitled to a November 13, 2019, priority date.

1 We have some applicable law citations here for Your Honors. If
2 we want to discuss them, we can, however, they're in our briefing. And
3 you're more than happy to answer any questions you may have on how we
4 view how the facts here fit into the case law.

5 Great. And just wanted to move on briefly, Your Honors, to slide
6 34. This was brought up by Mr. Patel. There was some discussion about the
7 brainstorming and the TTI and how that came about. To clarify the point
8 made in our briefing that opposing counsel relied on to say we're incorrect
9 that both Dr. Tardif and Bouabdallaoui are consistent. The Tardif statement
10 that's blanket. Yes, I am the sole inventor, which is at his deposition
11 transcript page 37, lines 9 to 18.

12 In this citation right here, where Dr. Bouabdallaoui says Dr. Tardif
13 suggested to a number of the members of his team to discuss any ideas they
14 come up with from the database. These discussions were led by Dr. Tardif.
15 He came to his colleagues with the ideas from those initial reports of the
16 COLCOT study, which were published -- those primary findings were
17 published in December of 2019 in Exhibit 1022 by Dr. Tardif in the New
18 England Journal of Medicine where again, Dr. Tardif is the corresponding
19 author.

20 And just briefly, Petitioner also asserts Ground 4 for the same
21 reasons that Bouabdallaoui is not prior art under Ground 1. It is also not
22 prior art on Ground 4 and therefore cannot be relied upon as an obviating
23 reference. The Colcris label itself is insufficient to obviate any of the
24 claims of the '063 Patent and we have not heard Petitioner make any
25 argument that they do.

26 And moving on to Ground 2, which is Petitioner's allegation that

1 the COLCOT protocol summary from ClinicalTrials.gov, which is at Exhibit
2 1006, does not anticipate Claims 27, 29-36, and 39. So firstly, really
3 important that you didn't hear from Petitioner. The updated version of the
4 ClinicalTrials.gov summary of the COLCOT trial was before the examiner
5 and was considered by the examiner.

6 Their own expert, Dr. Ridker, couldn't recall ever having seen
7 Exhibit 1006, yet he extensively opines that it both anticipates and in part
8 obviates the claims of the '063 Patent. Instead, he said he would look at the
9 full protocol, which the evidence at Exhibit 2069 shows was not publicly
10 available until July 16, 2020.

11 And really briefly, when we talk about those pieces of prior art and
12 arguments already before the Board, this is exactly the type of arguments
13 that was tried to be prevented by the Drinkware decision. We don't want to
14 repeat everything before the office over and over and over again. And that's
15 all that Ground 2 is, presenting the same argument with the same prior art.
16 And in fact, older prior art with less information.

17 Moving on to slide 42, as Your Honor pointed out earlier correctly,
18 Exhibit 1006 has no results. So, as Mr. Patel explained, the preamble to
19 Claim 27 and its dependent claims of reducing the risk of stroke should be
20 considered limiting. And because it's limiting, the fact that there's no results
21 as of this reference, this reference does not disclose what happens with the
22 risk of stroke in these patients. We don't know, we have to test it. And that's
23 what Dr. Tardif did and surprisingly discovered.

24 To try to plug this gap, very tellingly, Petitioner inserts at one of
25 their slides a different exhibit, Exhibit 1007. But that's not anticipation.
26 That's just another obviousness argument that they're trying to sneak in.

1 Similarly, we don't have inherency here. Inherency isn't simply an
2 invitation to investigate. And that's what Exhibit 1006 is. It is a description
3 to the world of the protocol that will be used in this study. It doesn't say
4 here's what's going to happen, because there's a lot of hypotheses in that
5 paper. And in fact, many of them were not met. Many of them were not
6 met.

7 Other contemporaneous art also shows in a very similar patient
8 population, under very similar circumstances, you get a different outcome.
9 Exhibit 2056 is the COPS reference. The COPS study was first published
10 the exact same day as Bouabdallaoui. It was presented at the exact same
11 conference. And Petitioner tries to differentiate it and say, well, that's with
12 acute patients.

13 Those patients in the COPS were initiated on colchicine within the
14 first seven days after an MI. They took it for one year. They did a
15 secondary analysis after the results were not positive, quote, in line with
16 those of the COLCOT study, and they still could not get statistical
17 significance.

18 The COLCOT study had more than 1,500 patients in that study
19 initiated within the first seven days. And across its entire cohort, it found a
20 decrease in the risk of stroke. Two studies completed at the same time,
21 publishing the results at the same time, opposite findings. Policy really also
22 urges the Board to not find inherency here. This would have a really chilling
23 effect on R&D, or alternatively, in overburdening the patent office.

24 If a protocol summary anticipates the findings of that study being
25 done years later, is what we're likely to see is either less clinical trials, or
26 alternatively, patent applicants filing applications on things that are not yet

1 enabled. File for all my hypotheses and go through the prosecution and
2 overburden the patent office until I get a negative result and withdraw, or I
3 get a positive result and I supplement my filing with new information.
4 That's not a tenable situation.

5 Similarly, the dependent claims are not anticipated by Exhibit
6 1006. None of those additional limitations are found in that reference.
7 Moving on to Ground 3. It's really important here to understand this prior
8 art combination. Petitioner relies on Nidorf, which is a patent, Exhibit 1007,
9 COLCOT, Exhibit 1006, the same reference we were just discussing, the
10 ESC Guidelines, Exhibit 1009, and the Colcrys label, Exhibit 1016.

11 All of these, or the very similar ones, except for the ESC
12 Guidelines, were already before the examiner. They were already
13 considered. They're duplicative. Examiner looked at these things and said,
14 yes, this is still entitled patentability. But we really need to understand too,
15 why Petitioner's analysis is so hindsight driven. And it's because they
16 started with the patent claims in '063. And they've gone back to these
17 studies and only picked the ones that support their theory. So they went
18 back to Nidorf.

19 Nidorf is a patent that was granted to Petitioner after the LoDoCo1
20 study. The LoDoCo1 study had patients that were initiated after they were
21 six months stable after an MI. So it's not six months after an MI. They
22 reached stability first and then waited six months at least and then initiated
23 them. And that's really critical. Because, one, as all the experts have
24 agreed, sometimes it takes patients up to 30 days or more to become stable.

25 Also during that entire time, secondly, all these patients are
26 receiving other existing secondary therapies. They're receiving statins,

1 blood thinners, aspirins, other drugs and medications to help reduce the
2 likelihood of a future MI event. And then they're given colchicine, which is
3 supposed to do it even further.

4 So this is exceptionally different patient class than what we saw in
5 COLCOT, where within 30 days after an MI, whether stable or not. And
6 similarly, the claims of the '063 Patent are stable agnostic. There's no
7 limitation requiring the patients to be stable. As Dr. Ridker admitted, as Dr.
8 Ardehali admitted, a patient may or may not be stable within three days.
9 They may be stable at day 10. and the patent claim doesn't say, oh, don't
10 give them the colchicine, and that's not what was found in COLCOT either.
11 There's no data differentiating on stability.

12 And that's why the LoDoCo study, and ultimately the Nidorf
13 Patent, we only pluck the things that work for Petitioners theory is how they
14 want you to operate. But even when we look at the loading dose, preferred
15 embodiment is to administer a loading dose. I don't disagree with Petitioner
16 that later in the patent there's also a citation in the specification in which
17 there's described no loading dose. That's in the description of the LoDoCo
18 trial. But yet they still put here and here preferred embodiment.

19 So Petitioner is saying ignore the stability difference, ignore the
20 preferred embodiment, just focus on this one thing. Well, how do you get
21 there? The claims of the '063 Patent. That loading dose was also the
22 standard of care. Petitioner wants to say pericarditis is unrelated. It's a CV
23 disorder. It was the only CV disorder in which colchicine has been used in
24 the prior art before the approval of LoDoCo. The only one. And there,
25 loading dose, standard of care.

26 The examiner found no motivation to remove the loading dose.

1 Importantly, this circulation 2015 reference is Petitioner's own reference,
2 Exhibit 1040, Deftereos. And the American Heart Journal is their own
3 reference, Exhibit 1028, NIC 2019. Again, the examiner's already dealt with
4 this, and yet here we are again.

5 The administration. There was not early administration motivated
6 by Nidorf. There's not early administration motivated by COLCOT. We
7 don't know the results of COLCOT protocol at the time of the patent. We
8 don't have those yet. Instead, all we have is this plan, this hope, right?

9 Finally, the ESC Guidelines. It says initiate certain drugs within
10 three days. So yes, administer colchicine early is what Petitioner says.
11 There's no basis for that. The only thing the prior at that time showed for
12 early administration of colchicine in CV patients was that it was not unsafe.
13 There was not a finding of efficacy until the COLCOT results and the
14 Bouabdallaoui 1005 and the '063 Patent. The '063 patent is the first time we
15 really see segmented in those first three days, it is safe and effective to give
16 colchicine to these post-MI patients.

17 And I finally want to briefly address Your Honor Judge Jenks'
18 question about not all patients are given the drug to reduce stroke. And to
19 clarify there, Your Honor, this is a circumstance in which all patients are
20 given the drug, right? We look at COLCOT. Everyone in the intervention
21 arm is given colchicine. Everyone in the placebo arm is given placebo as we
22 typically see.

23 And what the Claim 27 is instructing is that the result of following
24 the administration regimen is a reduction in the risk of stroke in the patient
25 population post an MI. That patient population after an MI, we already
26 know they have an increased likelihood of stroke as well as the other CV

1 events. So, by following the claimed administration, the result is that
2 population has reduced risk of stroke, which was entirely novel until the
3 COLCOT study. And if Your Honor has a follow up question, I'm happy to
4 address it.

5 JUDGE JENKS: I'm sorry, but how is the claims administration
6 different from the instructions in the COLCOT study? That's where I'm at.

7 MR. WILKERSON: Yes, Your Honor. They are not. And that's
8 what's different, is the limiting preamble. Without that preamble, the claim
9 is meaningless because otherwise you're just administering the drug to
10 patients that have an MI. To what end? It could be to any other secondary
11 hypothesis like diabetics, for example.

12 JUDGE JENKS: Okay. So if I'm giving -- if I'm giving colchicine
13 to a patient who has MI and I instruct them to do so and you know what, he
14 goes out and does it and therefore he has a reduced risk of stroke. Am I
15 infringing your claim? Because I'm using it, I'm giving it because he had
16 MI, not because he's getting a reduced risk of stroke. I'm giving it just
17 because he's had MI.

18 MR. WILKERSON: The single instance, Your Honor, I guess, is a
19 difficult differentiator because it's what we talk about with these claims and
20 with the studies is population-based rather than an individual basis. And so
21 if you're the attending and you do that with 100 patients, there would be
22 infringement because as the study results have shown that the likelihood
23 across the population is a reduced risk in stroke.

24 Specifically, it's from Bouabdallaoui, we have a reduction in risk
25 of stroke of 75 percent in the 0-30 day population. I'm sorry, 0-3 day
26 population. Relative risk reduction. Pending any further questions --

1 JUDGE JENKS: No, sorry. I was just saying Claim 27 doesn't
2 require me to give it within three days for the risk of stroke.

3 MR. WILKERSON: It's within 30 days, Your Honor, and there is
4 still a statistically significant reduction in the risk of stroke. I just pulled this
5 one up because this was the only exact figure I had presently handy. But if
6 you would like, I'm more than happy to pull the exact figure for you from
7 the Exhibit 1005.

8 JUDGE JENKS: All right. No need to do so, I can look it up
9 myself.

10 MR. WILKERSON: Certainly. Pending any further questions, I
11 yield the remainder of my time.

12 JUDGE JENKS: Excellent. Petitioner, you have 30 minutes for
13 your rebuttal.

14 MS. BROUGHER: Your Honor, do you mind if I speak to my co-
15 counsel before addressing the rebuttals?

16 JUDGE JENKS: How much time would you like?

17 MS. BROUGHER: One minute.

18 JUDGE JENKS: Okay. You may begin when ready.

19 MS. BROUGHER: Thank you.

20 JUDGE JENKS: All right, let's see if it loads.

21 MS. BROUGHER: Why is it not showing my PowerPoint?

22 JUDGE YANG: We actually have all the slides. If you need
23 slides for your sake, then let's work it out. Otherwise, you can continue.

24 MS. BROUGHER: That's fine. Thank you, Your Honors. I
25 would like to start with discussing inventorship again. And in particular, we
26 just heard testimony from Patent Owner's side that Dr. Bouabdallaoui

1 corroborated that Dr. Tardif is the sole inventor. But I would like to walk
2 you through slides 77-79 specifically, and these are the ones that come from
3 the deposition.

4 On slide 77, she says that it's not a one-person idea, and this kind
5 of discussions are kind of outcomes of brainstorming that take place. So as
6 far as I remember, it's not a one-person idea. Then she goes on to explain
7 the process with these brainstorming sessions. She goes on to say that
8 different members think about how to use information that is included in
9 COLCOT, and it is the framework of these kind of meetings that decisions
10 are made about the analysis to achieve.

11 Slide 77. She actually talks about Dr. Tardif's role in these
12 brainstorming sessions, and she says that Dr. Tardif suggested to a number
13 of the members of his team to discuss any ideas that can come up from the
14 database, and these are the brainstormings. Well, if Dr. Tardif asks his team
15 members to come up with ideas, I mean, that kind of shows you that the
16 ideas are coming from somebody other than Dr. Tardif. She does admit that
17 she does not remember who came up with the time to initiate treatment.

18 So she doesn't remember that, but she does talk about these
19 brainstorming sessions. And then she further elaborates, saying you conduct
20 a clinical trial, and that clinical trial in this case was COLCOT. You will
21 have a database with a lot of data, and then you ask yourself as an
22 investigator, what other questions can you get out of this data?

23 So this is, you know, this idea, we don't know who came up with
24 it. We are not saying that it's Dr. Bouabdallaoui. We just think, based on
25 what we have received from Dr. Bouabdallaoui, that somebody other than
26 Dr. Tardif came up with this 0-3 day time limitation. And that's all what

1 we're asking for here.

2 We don't care about who came up with COLCOT, who recruited
3 investigators. We're concerned about this 0-3 day time period, and who
4 came up with that specific time period, because that is the crucial
5 information here. It's not about the COLCOT trial.

6 And we also heard from Patent Owner about this Katz declaration,
7 and today's the first time we heard them refer to what we think is Dr. Tardif's
8 first declaration as a Katz declaration. I don't think that's a Katz declaration.
9 It has no discussion of conception. It doesn't have all the details necessary
10 for it to be a Katz declaration. And there's also no truth statement to it.

11 So at best, it could be considered an attempt at a Katz declaration,
12 but it's still, it's not what we need for this fact-intensive analysis on
13 inventorship. So that's all I want to say about inventorship. But let me also
14 go back to Ground 2 and talk about antecedent basis on slide 14.

15 Now, I will admit that I'm a patent prosecutor by training. So for
16 me, getting to the preamble of this claim requires a lot of effort, because
17 there are just so many problems with this claim, and one of the problems is
18 this antecedent basis. So Patent Owner points to, in the body of the claim,
19 the patient, and suggests that because you have the word the patient, that
20 refers to the preamble, and that's where you get your antecedent basis, and
21 that's why the preamble should be limiting.

22 But if you look at the body of the claim, you also see the word the
23 administration. That word the has no antecedent basis in the preamble. You
24 also see the word an MI. And in that case, MI was already in the preamble
25 itself. So, you know, again it's just poorly written claim at the end of the day
26 that is anticipated by the 1006 reference.

1 I would also like to point out that we're a little confused with
2 Patent Owner's allegation that the dating of 1006 is inappropriate. They
3 make some comments about the internal dating being 18 months after what
4 our librarian declarations say it is, and we're a little confused about that 18-
5 month date.

6 But what we believe it is referring to is some other document,
7 some other version of the protocol that is 18 months later. But 1006 is dated
8 according to what our librarians say it is dated, and we see no reason to
9 believe otherwise.

10 I would also like to clarify Dr. Ridker's confusion about 1006. Dr.
11 Ridker knows the COLCOT protocol inside and out. He knows it better than
12 almost anyone. For his own purposes as a primary or a principal
13 investigator or as a physician, he would refer to the full protocol when
14 analyzing something or conducting a clinical trial.

15 What we're referring to as a protocol, 1006, is technically not a
16 protocol. It is just a brief summary that's found on ClinicalTrials.gov. What
17 he refers to as a protocol is something else. We did try to clarify his
18 statements in the second declaration that he submitted. I would also like to
19 take a moment to clarify the COLCOT trial.

20 JUDGE YANG: Before you go on, I'm still staring at Claim 27.

21 MS. BROUGHER: Sure.

22 JUDGE YANG: I hear you saying the preamble is not limiting,
23 but during your opening you also said even if it is limiting, the prior art
24 would still teach or disclose this. I believe you mentioned inherency at that
25 time. Did I remember it correctly?

26 MS. BROUGHER: Are you referring to slide 15 by any chance?

1 JUDGE YANG: I'm at slide 14 is, correct.

2 MS. BROUGHER: 14, yeah. So, both. So for purposes of
3 Ground 2, we're looking at inherency. So you just have to look at the steps
4 of the method and ask the question of whether or not, if you practice the
5 method and give colchicine, will you inevitably get risk reduction in stroke?
6 The answer is yes from a one or two perspective for anticipation. But even
7 kind of as a side note, we already knew that from the LoDoCo trial several
8 years prior that administering colchicine to patients will result in a stroke
9 reduction.

10 JUDGE YANG: Okay. So inherency, we're talking about
11 necessarily would result in the reduction, right? If I understand counsel for
12 Patent Owner correctly, they mentioned that there was some other
13 publication on the same date that actually disclosed the opposite result. Do
14 you understand what I'm referring to?

15 MS. BROUGHER: Yes, you're referring to the COPS publication
16 analysis.

17 JUDGE YANG: Okay. Could you address that, please?

18 MS. BROUGHER: Gladly. So let's turn to slide 45, for instance,
19 or even 44. On slide 44, Dr. Ridker went through all of these other
20 references that allegedly show that there's some unpredictability in the art,
21 and he grouped them according to what he believes is accurate. So there's
22 one study, and it is the COPS study, that has a clinical endpoint but it is
23 directed to unstable patients with acute coronary syndrome.

24 There's three studies, the LoDoCo, COLCOT, LoDoCo2, that have
25 the clinical endpoints and look at stable atherosclerotic disease, which is
26 what we've been talking about. Then this next group, which Patent Owner

1 points to, that includes Hennessey, Raju, and Akodad, that's the COLIN trial,
2 those are all surrogate endpoints, and they're surrogate endpoint's usually
3 looking at the CRP biomarker, and that is a substitute for looking at
4 inflammation and the state of inflammation resulting from the acute event.

5 But regardless, these are 30-day studies looking at this biomarker
6 and asking whether or not there's this reduction of inflammation from the
7 acute event. That's not what we're talking about in terms of these patient
8 populations. We're looking at the chronic atherosclerotic disease that
9 patients live with. And if you want to think about it kind of differently,
10 when somebody has an MI event or even a stroke, that's the event itself, and
11 that triggers an inflammation that stems from that event.

12 And that inflammation, kind of even like in gout or FMF, that
13 inflammation will ultimately subside whether it's 30 days or whatever else,
14 but that inflammation subsides at some point. What we're talking about is
15 the chronic atherosclerosis that the patients continuously live with, which is
16 a different mechanism than what we have with the acute phase.

17 And what we're seeing so far is colchicine acts on that long-term
18 chronic atherosclerosis, and these studies at best support the hypothesis that
19 probably colchicine does not act upon that acute inflammation that we see
20 kind of after an event takes place. But regardless, we're looking at apples
21 and oranges here. We're not looking at the acute inflammation that's taking
22 part. We're looking at that underlying disease, like a quiet disease that
23 people like you and I live with all the time and that we have in our body.

24 So that's the quick way of separating out those studies. And
25 COPS, for instance, on slides 46 and 47, quite frankly, we're not sure what
26 Patent Owner is arguing with COPS. They have submitted COPS in support

1 of their regulatory filings together with LoDoCo and COLCOT and
2 LoDoCo2. What we're seeing here, though, is that we had different patients.
3 So again, COPS is looking at these acute coronary early-stage patients.

4 They had a different dosage amount. It was basically double the
5 dose of colchicine. They also had a different follow-up, and they also had a
6 different primary outcome. In COPS, they were looking at all-cause
7 mortality rather than just from cardiovascular events.

8 So what we do know from everything we've seen here, from
9 everything Dr. Ridker has said, when we're looking at patients with chronic
10 atherosclerotic disease who are stable, who are no longer treated in the
11 hospital, these patients can leave the hospital, colchicine on them is going to
12 work no matter when you start the treatment. This is a drug that is meant to
13 be given to patients for a long period of time, 2, 3, 4, you know, 10 years,
14 whatever it is. So it makes sense to start it as early as the patient is
15 stabilized.

16 JUDGE YANG: Thank you.

17 MS. BROUGHER: So I think one additional point that I just
18 wanted to clarify because we heard about it. The COLCOT protocol, and for
19 some reason nothing is showing up, but I can point you. This is the 1006
20 reference. If you look at the bottom of page 4, top of page 6 -- 5, sorry, you
21 are going to see the inclusion and exclusion criteria for COLCOT.

22 So COLCOT patients, third bullet point down, must be treated
23 according to national guidelines including anti-platelet therapy, statin
24 therapy, renin-angiotensin-aldosterone system inhibitor therapy, and beta-
25 blockers. So these are patients who are undergoing other -- are being treated
26 with other secondary therapies. This is exactly the same as LoDoCo.

1 And this trial specifically excluded patients, if you turn to the top
2 of page 5, patients with poorly controlled medical condition, patients in
3 cardiogenic shock, or with hemodynamic instability. I mean, these were all
4 stable patients who could have been dismissed from the hospital. I have no
5 further comments.

6 JUDGE JENKS: Okay. I do not have any other questions.

7 MR. WILKERSON: Ready when you are, Your Honors.

8 JUDGE JENKS: Please go ahead when you're ready.

9 MR. WILKERSON: Thank you. Just to briefly address some of
10 the comments from Petitioner, I first want to point to this slide 44 from
11 Petitioner's demonstratives, and it's really important to point out a few
12 characteristics here. Firstly, these are Dr. Ridker's characterizations of the
13 studies. This is how he's viewed them. He's opined on what Exhibit 1006
14 says about inclusion and exclusion criteria.

15 And exclusion criteria, as counsel is pointing out, patients with
16 cardiogenic shock. What is that? That's a patient with such severe shock,
17 such low blood pressure after something like an MI. They're in the ICU.
18 They're not commonly going to be the subject of a clinical study unless that
19 clinical study is to test ways to treat cardiogenic shock. We cannot be
20 risking the lives of those patients.

21 So that does not mean that we have stable patients in COLCOT. In
22 fact, if we look at the New England Journal article that publishes the original
23 findings of COLCOT, Dr. Tardif himself talked about why he conducted the
24 COLCOT. It was because he saw that LoDoCo was deficient in several
25 ways.

26 He also says here, quote, because acute coronary syndromes are

1 associated with higher risks of recurrent events and exacerbated
2 inflammation, we conducted the COLCOT trial to evaluate the effects of
3 colchicine on cardiovascular outcomes as well as its long-term safety profile
4 in patients who had recently had a myocardial infarction.

5 He specifically saw that LoDoCo was only with patients that had
6 been long-term stabilized. It had been non-placebo controlled. It was not
7 randomized. It was open-label. It had a small population. So he undertook
8 the COLCOT study to fix this. And this is from Exhibit 1022 at page 3.

9 Similarly, the COPS trial, when discussing the other trials that had
10 come before it, the COPS authors in Exhibit 2056 at page 2 describe, both
11 the COLCOT and LoDoCo trial demonstrated a significant reduction in
12 adverse cardiovascular events in patients with ACS. Again, ACS, acute
13 coronary syndrome, is COLCOT, as the authors of COPS said, as the authors
14 of COLCOT say, as everyone other than Dr. Ridker has opined.

15 And again, the purpose here of the COPS was wanting to look at a
16 broader category, and that's why in the COPS study those researchers
17 decided to look at all-cause mortality. They did it at the one-year mark.
18 Really, they did it at the one-year mark because they had a predetermined
19 time at which they hit that all-cause mortality once enough patients died.
20 That's how we do all-cause mortality studies.

21 So it's not that they just decided, oh, we want to do it at that period.
22 No, that's when they got their significant figures to be able to produce
23 results. And they found that there was no improvement, right? And they did
24 give a loading dose, because as we've said, this was initiated in the prior art,
25 even though the results were published thereafter. And in the prior art, the
26 standard of care in the acute setting of colchicine was to give a loading dose.

1 That was how it was always done.

2 The COPS study has an extremely similar population, ACS. While
3 some -- and, again, as all the experts in this case have testified, there was no
4 requirement explicitly stated in COPS that the patients be unstable. It was
5 just within that first week. So as all the experts have already testified, there
6 would have been stable patients in that population, just like there were some
7 stable patients in COLCOT, but also unstable patients.

8 Contrary to both the LoDoCo trials, LoDoCo1 and LoDoCo2,
9 where patients had to be stabilized for six months, receiving all these other
10 therapies that bring them back to healthy, that have been approved for years
11 and shown to be relatively effective. The one time that Petitioner attempted
12 to do low dose colchicine in the acute setting was Hennessey, the LoDoCo
13 MI study, Exhibit 1028. They initiated that shortly after MI, and they
14 continued it for 30 days and they found it was not effective at controlling
15 high-sensitivity CRP.

16 Petitioner says that's a biomarker, it doesn't matter. That's the
17 same pathway and biomarker that their expert, Dr. Ridker, testified he's
18 dedicated his life's work to. His CANTOS trial found that connection
19 between these protein pathways that cause inflammation, and this
20 inflammation that that his CANTOS research suggests can be specifically
21 addressed to treating CV and reducing the likelihood of future CV events, is
22 what they're saying the art you can disregard.

23 Disregard because it's a biomarker rather than a clinical endpoint.
24 That's not true. It is a surrogate, but it's the most relevant biomarker if we
25 want to accept Petitioner's primary and base premise that the CANTOS trial
26 is what confirms and sends us down this path of everyone in the prior art

1 knowing, oh we can target specifically inflammation.

2 So if we ignore those biomarker studies which showed an
3 effectiveness other than CANTOS using a different drug, then we must
4 exclude CANTOS, we must exclude that at the time in the prior art. A
5 POSA would have expected that specifically targeting inflammation would
6 be effective, because the only time it was shown was in an open label, non-
7 randomized, small population study in patients that were stable for six
8 months.

9 Briefly back to inventorship. As we heard from counsel, the main
10 issue here is really prior art. The issue here is, is the Bouabdallaoui
11 reference, Exhibit 1005, prior art? And how we got there, as I mentioned,
12 was first, Petitioner says it's prior art because of priority date in their
13 petition. We respond in our POPR that is not prior art because of the
14 priority date you're asserting is incorrect, and because it's the work of Dr.
15 Tardif, the inventor, one year before the grace period at the latest possible
16 priority date.

17 Their rebuttal to that was, no, Dr. Bouabdallaoui is. You just have
18 Dr. Tardif's uncorroborated claim that he is the author. And then from there
19 we snowball into this sideshow of inventorship. But that's not really the
20 question here. The question here is whether Exhibit 1005 is prior art, and
21 unequivocally the answer is no. The proper priority date is November 2019.

22 Even if the Board were defined that November 2020 is the correct
23 priority date, this paper Bouabdallaoui referenced, Exhibit 1005, was done at
24 the direction of Dr. Tardif. Both witnesses said it was done at the direction
25 of Dr. Tardif. They don't see it here in pages 77 and 78 with excerpts from
26 Dr. Bouabdallaoui's testimony at deposition. But if you go back and look at

1 the record, she testified several times.

2 The person who received the statistics report from the statisticians
3 who were directed to do the study, directed to do the post hoc analysis, was
4 Dr. Tardif. After that analysis, Dr. Bouabdallaoui collaborates with him,
5 which is very acceptable. The Supreme Court recognized that back in the
6 1850s with the Morris case and dealing with inventorship, with the telegram.
7 We decided that it's not necessary for an inventor to isolate themselves to be
8 the inventor. It's just that the conception is theirs. And that's what we have
9 here.

10 And the only evidence, the only thing that consistently Petitioner
11 points to is the author heading on Exhibit 1005. And then they say we have
12 not met our burden. That is not the case and that is distracting from the
13 issue. Pending any questions, I have nothing further and appreciate Your
14 Honors for your time.

15 JUDGE SNEDDEN: I have a couple questions. Just mainly
16 clarifying questions. I want to make sure I understand your positions. Now
17 when we look at Claim 8, for example, and you talk about the importance of
18 whether the patients are stable versus unstable, that's really getting to the
19 claim element with it that is within about three days of MI. And just to
20 make sure I understand what we're saying there is that after having an MI,
21 within three days that the patients aren't stable. So we're looking at an
22 unstable population. Is that the position?

23 MR. WILKERSON: The position is that the claim is agnostic to
24 stability. It doesn't matter. We don't -- in fact, we wouldn't have filed for
25 that because we don't have the data to enable a claim that they must be stable
26 or must be unstable. Because what the data shows us is that within three

1 days of an MI, if we initiate the treatment, we see the claim reductions and
2 see the events thereafter.

3 So some of those patients may be unstable, something may be
4 stable. We don't know. And the point we were raising there was Dr.
5 Ridker's analysis, Petitioner's expert, inserts that stability claim limitation as
6 a requirement. So when he says his arguments for a priority date, he's
7 inserting that limitation, which doesn't exist.

8 JUDGE SNEDDEN: Okay, understood. I'm glad I asked that.
9 Okay. One more question. Also, we're looking at, say Claim 8 I believe,
10 and then Ground 3. The claims require preloading the patient with a higher
11 dose of the -- how do you say it again?

12 MR. WILKERSON: I'm sorry, colchicine?

13 JUDGE SNEDDEN: Colchicine. At page 37 of the petition, the
14 petition does go into some analysis and show exactly -- they make the case
15 that neither Nidorf or the COLCOT protocol requires preloading. How do
16 you address that?

17 MR. WILKERSON: Certainly. So the difference there, Your
18 Honor, is in the Nidorf reference itself, which is what Petitioner chose to
19 rely on, on his prior art reference. There's also the preferred disclosure of a
20 loading dose, right? So if they wanted to instead rely on the LoDoCo study,
21 they could have, but they didn't.

22 So even if we say that Nidorf teaches no loading dose because it's
23 silent, Patent Owner's expert, Dr. Ardehali, explained at deposition and his
24 declarations how a POSA would regard a difference between an explicit
25 instruction to have a loading dose, silence, and an explicit instruction not to
26 have it. They're not quite all the same, And that's how a POSA would view

1 those things, right?

2 So then is what we're left with is the claim says explicitly not to
3 have a preloading dose. Why is that different from Nidorf? It's because if
4 we look at the claim as a whole, it's within that three days limitation. As we
5 saw with COPS, those researchers call in trial. They said, oh, we failed in
6 the acute setting because we didn't have a preloading dose.

7 COPS, they tried a preloading dose in the acute setting because
8 they thought that's what was needed, because as Dr. Ardehali testified,
9 pericarditis, they do a preloading dose and they have because they need to
10 jumpstart the inflammation in that acute setting. That's not what happened
11 in LoDoCo or Nidorf because there's no acute setting. That patient's been
12 stable for six months. Their inflammation and their hs-CRP has
13 substantially decreased across that six months from the other therapies.

14 JUDGE SNEDDEN: Okay, thank you. Understood.

15 MR. WILKERSON: You're welcome.

16 JUDGE JENKS: I don't have any further questions, and I think the
17 rest of my panel -- Judge Yang, you have any other questions?

18 JUDGE YANG: No.

19 JUDGE JENKS: Okay. Well, then I want to thank the parties for
20 appearing today. We especially thank our LEAP practitioners participating
21 in this oral hearing. This case has now been submitted to the panel, and we
22 will issue our decision in due course. And with that, the hearing today is
23 adjourned. Thank you so much.

24 (Whereupon, the above-entitled matter went off the record at 3:37
25 p.m.)

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