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EDITED TRANSCRIPT

MRNA.OQ - Moderna, Inc. - Special Call

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PRESENTATION

Operator

Good morning, and welcome to Moderna's American Society of Clinical Oncology Review Call. (Operator Instructions) Please be advised that the call is being recorded.

At this time, I'd like to turn the call over to Lavina Talukdar, Head, Investor Relations at Moderna. Please proceed.

Lavina Talukdar - *Moderna, Inc. - Head of IR*

Thank you, operator. Good morning, and welcome to Moderna's ASCO 2019 update call. On today's call, we will review interim data from our Phase I personalized cancer vaccine study that was presented at the American Society of Clinical Oncology meeting over the weekend. You can access the press release issued as well as the studies that we'll be reviewing by going to the investors section of our website at www.modernatx.com.

With me on this call is Stéphane Bancel, Chief Executive Officer; Tal Zaks, Chief Medical Officer; and Lorence Kim, Chief Financial Officer.

Before I begin, I would like to remind everyone that this conference call will include forward-looking statements. Please see Slide 2 of the accompanying presentation of our SEC filings for important risk factors that could cause our actual performance and results to differ materially from those expressed or implied in these forward-looking statements. We undertake no obligation to update or revise the information provided on this call as a result of new information or future results or development.

I will now turn the call over to Tal.

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you, Lavina. Good morning, everybody. It's a real pleasure to welcome you from ASCO Chicago where I'll be describing our first interim analysis of our Phase I open labeled study to assess the safety, tolerability and immunogenicity of our personalized cancer vaccine, mRNA-4157, that is being conducted either as a single agent in patients with adjuvant resected solid tumors or in combination with pembrolizumab in patients with metastatic disease. As a reminder, this study also has a keynote number of KEYNOTE-603, which is reflective of our ongoing collaboration with Merck on this program.

Let me spend a minute on the background for our therapeutic approach. We know that it is mutation-derived epitopes in tumors that are important in activating T cells that then drive antitumor responses. We've learned this from the success of the field of the checkpoint inhibitors. And we have

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hypothesized that vaccinating patients against so-called neoepitopes or neoantigens in combination with a checkpoint inhibitor should elicit a greater antitumor response than just the checkpoint inhibitors alone would.

Now the challenge is that these mutations are almost never shared between patients. So if one were to do this, you would need a personalized approach to the cancer vaccine where every single vaccine is uniquely designed and manufactured. And this is what we've done. MRNA-4157 is a personalized neoantigen cancer vaccine that is created by determining the mutations in each patient as well as the genotype of the major histocompatibility complex, or MHC, of their immune system. The MHCs present antigen to T cells. We then select these neoepitopes that we believe are most likely to activate that patient's set of MHCs and thus T cells.

So once we design each individual's unique vaccine, we then formulate it with our proprietary lipid nanoparticle delivery technology, make it in our Norwood facility, test it, release it and send it back to the patient to be administered. Our usual turnaround time for these vaccines has been in the order of 50 to 60 days from the time the tumor's biopsied until the vaccine is administered to the patient.

The patients that I will be describing in the current study have received vaccines with up to 20 neoantigens in a single administration. Recall that we increased the number of neoantigens in our current PCV vaccine. Patients enrolled in the study from April 2019 onwards have been administered their personalized cancer vaccine that encodes for up to 34 neoantigens, although we do not yet have data from those.

On Slide 6, you see the study design of our Phase I, where, in both parts, we've been treating patients with non-small cell or small cell lung cancer, melanoma and other tumors that are expected to have some response to checkpoint inhibitors alone. The objectives of this trial were to demonstrate the safety and tolerability of mRNA-4157 both as monotherapy and in combination with pembrolizumab. We looked at the immunogenicity by assaying for neoantigen-specific T cell responses after a few cycles of therapy and we followed the clinical activity.

The study design is such that after a screening period, patients in the combination therapy arm will start to get pembrolizumab during the time in which we are manufacturing mRNA-4157. Our goal is to get them the vaccine to be taken together with pembrolizumab, starting at the third dose of pembrolizumab. We then continue treatment for up to 9 cycles of the combination. Note that we count cycle 1 as the start of the combination with both pembrolizumab and the vaccine. Patients, of course, can continue pembrolizumab monotherapy afterwards. It is much simpler for patients on the monotherapy arm for mRNA-4157 where they simply get their vaccine when it is ready. These are patients whose disease has been resected and mRNA-4157 is given in the adjuvant setting.

Let me talk a little bit about the patient demographics here. This is a typical Phase I population. You can see the majority of the patients are pretty heavily pretreated and there is no one histology that stands out. It is worth noting that the most frequent disease type that we see in this trial is non-small cell lung cancer, whether it's in the adjuvant setting or in the metastatic setting, followed by patients with bladder cancer, melanoma and other tumor types.

So let me start with the safety data, and the safety data here is collected following monotherapy of the vaccine in Part A and in Part B after the first couple of doses of pembrolizumab monotherapy and again, after administration of the combination of our vaccine with pembrolizumab. We did not see any mRNA-4157-related Grade 3 or Grade 4 adverse events and we did not see any serious adverse events. We also did not find any dose-limiting toxicities.

I should note that the data represent patients who were treated with all dose levels of our vaccine, starting at 0.04 milligram all the way up to the 1-milligram dose, at which we've only treated 5 patients thus far. So these are early days, but in totality, the data would suggest that this vaccine is well tolerated.

Let me now turn to the immunogenicity that we are seeing. What we did here was employ the usual method of assessing immunogenicity, which is stimulating T cells from the patient with the specific peptide epitopes in each patient's personalized vaccines.

I'm showing you on Slide 10 data from the first patient who was treated at 1 milligram in Part A, the adjuvant arm. So it is 1-milligram monotherapy of the personalized cancer vaccine. And the way we assess immunogenicity in this study is to collect peripheral blood and then stimulate T cells ex vivo following a few rounds of in vitro expansion to better refine the picture.

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The small volume of a peripheral blood draw limits the number of assays we can run. So what we've done here in this study is to take neoantigen pools of 5 epitopes each so that we can use the blood more efficiently. So for a vaccine of 20 epitopes, you will see 4 pools. And what we're measuring is the reactivity of these T cell against the patient's own dendritic cells when they're pulsed with pools of synthetic neoepitope peptides.

On the left, you see what is called an ELISpot assay looking at immunogenicity of the total cells taken out of the blood and this is without restimulation. On the graph on the right, you see following in vitro restimulation, we can now start to assay for CD8-positive T cells. So what is notable in this first patient at the 1 milligram dose is that we see a specific T cell response to every one of these pools seen after 4 cycles of treatment with the vaccine compared to baseline.

Now on Slide 11, we're showing data from the same patient, but this is with a different, more refined assay. Here, what we did was to conduct lymphopheresis in order to get a more granular picture of how many of these epitopes we're actually able to immunize against one-by-one.

Lymphopheresis is a procedure in which one collects lymphocytes out of the blood to a much more significant degree that can be obtained with just a regular peripheral blood draw. To give you a sense of comparison, apheresis procedure produces about 300x more lymphocytes than you can get out of 100 milliliters of peripheral blood. So when we do that, we're able to do much more refined and granular studies since we now have enough cells to stimulate the patient's T cells against each individual epitope. We can also do a more refined characterization of what kind of T cells we get.

And so on this slide, you can see that if we look at the x axis across the totality of the 20 epitopes that were in this patient's vaccine, we had 15 of these epitopes that were predicted justifying to Class I and we had 2 epitopes that were predicted justifying to Class II. And notably, 3 would have been predicted to bind both the Class I and Class II. This potential dual affinity to both classes is possible within mRNA-based vaccines because we include the sequence for longer potential epitopes and the patient's own immune system will then select whether to present it to a Class I or Class II major histocompatibility complex allele.

And so if you do the math, you can see that we're able to stimulate against 10 of the 18 neoantigens that are predicted to bind to Class I MHCs. Moreover, we're able to induce interferon gamma-secreting CD8-positive T cells. And the way we run this analysis is by typical flow cytometry so that we know that the cells we're stimulating are now actual CD8-positives, the kind of cells that you would hope would have a cytolytic activity against cancer.

The final point that is worth making is that it turns out all of those epitopes against which we were able to elicit T cell responses had a predicted binding affinity of less than 500 nanomolar. On one hand, this isn't surprising as we believe these are the ones more likely to elicit a response, but it's gratifying to begin to validate it as one of the many neoepitope selection criteria that we use.

So turning to the clinical data, let me make a couple of observations. First, this is a very small clinical data set comprising very different histologies and patients who were treated both in the adjuvant setting as well as in the metastatic one. So obviously, we do not draw any definitive conclusions from this data set. In addition, you will see on Slide 12, these patients were treated with varying doses of our vaccine, given this is the first Phase I experience.

What you can see here is that the so-called swimmer plots that are the clinical outcomes for these individual patients. They are color-coded by the dose of vaccine, with dark blue treated at 0.04 milligram, red at 0.13 milligram, light blue at 0.39 milligram and finally green at the 1-milligram dose. The solid lines show the duration of administration of vaccine while the hatched bars represent those treatment follow-up. Of the 13 patients treated in the adjuvant setting, 11 remained disease free up to 72 weeks on study.

Moving over to Slide 13 and what we saw in patients with metastatic disease who received a combination of mRNA-4157 with pembrolizumab. Here, you can see in solid lines the duration of administration of the mRNA vaccine in combination with pembrolizumab; and then, in the hatched bar, those who continued on pembrolizumab alone. As you can tell, these are very early days, especially at the higher dose levels.

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We did see some clinical activity, so let me go through that in a little bit more detail. Of these 23 patients, 20 of them actually received the combination of mRNA-4157 and pembrolizumab. One of them, a colorectal cancer patient that was MSI high, had a complete response on pembrolizumab before we administered our vaccine which is obviously a terrific outcome for that patient.

We did see 5 patients with a partial response to the combination of mRNA-4157 and pembrolizumab. Interestingly, 2 of the 5 had progressed with prior checkpoint inhibitor therapy.

As of May 10, 10 patients remain on study, including patient 40038, who is deemed initially a pseudoprogressor; and patient 40040, who had a new lesion which then improved post subsequent follow-up. Both of these patients remain on study as of May 10.

So in total, out of the 20 patients that are evaluable for responses, we see 5 partial responses to the combination of our personalized cancer vaccine and pembrolizumab. Of course, this is a very small data set and early data, so it would be inappropriate at this time to even try and put a percentage on what this response rate is. But let me share some of the stories of these patients that are on our trial.

Slide 15 shows patients 40019, a patient with small cell lung cancer who was previously treated with chemoradiation and prophylactic cranial irradiation. And after 2 cycles of combination with mRNA-4157 at the 0.13-milligram dose that followed the first 2 monotherapy pembrolizumab doses, this patient did appear to have a partial response as you can see here in cycle 3 and then again in cycle 6. Unfortunately, they later had progressive disease because of enlargement of a non-biopsied lesion.

Patient 40023 is a patient with bladder cancer. Now this patient had multiple lines of chemotherapy, a frontal lobe resection for brain metastases as well as checkpoint inhibitor therapy that included 4 cycles of the PD-L1 inhibitor, atezolizumab. After entering our study with 2 initial cycles of monotherapy pembrolizumab followed by 2 additional cycles of the combination of our PCV at 0.13 milligram with pembrolizumab, this patient has had a partial response. As you can see here from the scans, where cycle 3 denotes the start of the third combination cycle, there are very clearly 2 large lesions in the lung that appear to be decreasing. This patient has continued to improve and remains on study.

Finally, patient 40031 is another patient with small cell lung cancer who was previously treated with combination chemotherapy. After 1 cycle, the first cycle of pembrolizumab, this patient had an immune-related adverse event which led to discontinuation of pembrolizumab, and subsequently, they were treated only with mRNA-4157 now at a dose of 0.39 milligram. This patient had a partial response at the first post baseline scan and remains on disease with a partial response.

So in conclusion, mRNA-4157 appears well tolerated so far at all the dose levels we've studied, with no dose-limiting toxicities, no Grade 3 or 4 adverse events and no serious adverse events reported thus far.

We can see neoantigen-specific CD8-positive T cell responses at 10 out of the 18 Class I neoantigens and patient 40033, which is the first patient dosed with 1 milligram as monotherapy and for whom we have apheresis data. It is notable that 100% of the positive -- CD8-positive T cell responses were to neoantigens with a high predicted binding affinity.

I would note that in our poster session, there was also a poster presented by the National Cancer Institute using our mRNA personalized cancer vaccine technology to include sequences that the NCI designed and administered as monotherapy in an independent clinical trial. They described 4 patients treated with a safety profile that is consistent with what I've described. And in 3 patients in whom they assessed immunogenicity, they were able to demonstrate the ability to elicit specific T cell responses against neoantigens. They did not see clinical responses to monotherapy of the vaccine in these 4 patients.

Overall, the safety, tolerability and immunogenicity data, especially when you take it in context of what we know about the immunogenicity of our mRNA technology in the context of several infectious disease vaccines, support advancement of mRNA-4157 to our previously described Phase II at the 1-milligram dose level.

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Lastly, I've described some clinical responses which in totality have been seen in 6 out of 20 patients treated in the combination. One response clearly is a response to pembrolizumab monotherapy. And of the remaining 5, 2 have been seen in patients who have been treated with either a PD-1 or a PD-L1 inhibitor, one of which we presented the CT scans for. I do not currently have scans available for the second patient.

In terms of the next steps. While we continue the expansion arms of the current Phase I study, we're in the process of launching the randomized Phase II study in the setting of adjuvant melanoma as we have described in the past. This Phase II study is designed to demonstrate the additive benefit of our personalized cancer vaccine to pembrolizumab monotherapy. This trial will enroll approximately 150 patients with melanoma in the adjuvant setting, where we intend to give the combination therapy to 100 patients with 50 in the control arm being treated with pembrolizumab monotherapy, per its approved label.

Clearly, this is a small study and we've set a high bar for ourselves. But I believe it is the right setting in which to demonstrate the potential clinical benefit of the immunogenicity we described here today.

In closing, I want to thank the patients, families, physicians, clinical trial site teams for participating in the study and helping us learn as much as possible about the potential of mRNA personalized cancer vaccines at this very early stage of development. Every one of the scans I shared is of a patient battling cancer, and I am eternally grateful for them to be part of our collective journey to try and improve outcomes from this grievous disease.

Let me now turn the [floor] to Stéphane.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Thank you, Tal. Good morning, everybody, and thanks for joining. We are very pleased with this interim clinical data analysis presented Saturday at ASCO and look forward to learning more in the Phase II study with Merck.

Before we move to Q&A, I wanted to take this opportunity to talk about these new clinical data in the context of our overall company strategy. As you know, Moderna currently has 21 development candidates in its portfolio with 11 in clinical studies. Across Moderna's pipeline, more than 1,000 healthy subjects and patients have been enrolled in clinical studies so far.

With this interim PCV Phase I data, we have generated critical positive results in 4 out of the 6 modalities with the over 2 modalities, the ones on the far right on the slides, moving towards Phase I results. In the first 4 modalities, where we now have human data: Infectious disease vaccines, cancer vaccines with today's data, intratumoral, localized therapeutics with VEGF.

We have shown a large body of clinical data that is consistent. We are following 4 features of Moderna's mRNAs platform: one, Moderna's mRNA investigational medicines have been shown to be safe and well tolerated; two, we have shown dose-dependent pharmacology; three, Moderna's practice encodes the correct protein we design in the mRNA; and four, the proteins made by Moderna's mRNA investigational medicine are functional in humans. These results speak to the quality of the science of our mRNA platform and are investigational medicines.

I would like to thank and congratulate the Moderna team in both Cambridge and Norwood for their relentlessness to deliver on our mission for patients. I'm very proud and thankful for their work which has led to this interim Phase I PCV data in our first presentation at ASCO.

With that, we are happy to take your questions. Operator?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) And our first question comes from Matthew Harrison with Morgan Stanley.

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Matthew Kelsey Harrison - *Morgan Stanley, Research Division - Executive Director*

I guess 2 for me. One, can you just talk in a bit more detail how the data informed dose selection? Was it just the safety profile or anything in terms of CD8/T cell expansion or something like that, that helped you think about dose selection?

And then the follow-up would be, you've expanded from 20 to 34 neoantigens. You've got these responses to a percentage of those in this study. Was the expansion just driven by your technical change at your ability to go higher? Or do you think you can generate more antigen responses by going more neoantigens?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you, Matthew. Let me answer these in orders. The question on dose selection is a good one and obviously, one we've thought long and hard about. I think there's a couple of components here for me that converge. The first is that we clearly see a level of immunogenicity that is robust, and I think it is supported by the ability to -- of having seen immunogenicity also at lower dose levels. And I refer you to the NCI's poster as one example of that; there, 4 patients were treated at doses of 0.13 and 0.39.

The second component for me is the safety and tolerability overall, which as you've seen, allows us to take it to 1 milligram. And we could potentially go higher, but the immune system has a threshold effect.

And I think the final element that makes me comfortable with this dose is the fact that it is a very similar formulation, the same components that go into our infectious disease vaccines. And there, we've seen immunogenicity from doses as low as 25 to 100 microgram. And from the data we've seen in the studies so far and that we've shared, you can see that we typically plateau at 100 to 300 micrograms. So I think giving 1 milligram and giving it repeatedly every 3 weeks, although the infectious disease studies are obviously -- you measure it by antibody responses, but that magnitude of response that we consistently see in the infectious disease setting would lead me to believe, although I don't have direct data, that there is also a T cell component that is supporting that.

And so if you take what we know in total about the platform, if you take what we've learned in our hands and the NCI hands about immunogenicity and if you take a look at the safety and tolerability that we see, both here at the 1-milligram dose and in the 1,000-subject healthy people overall that we've dosed to date across the infectious disease, 7 Phase I trials, I think the 1-milligram dose is one that makes sense.

It's very hard to define a dose response curve when your assay requires apheresis and when every patient receives their own vaccine. Some component of immunogenicity will be a function of how many mutations there are, and some component of immunogenicity will likely be a function of the patient's specific MHC and our ability to predict binding.

And so that takes me to your second question. The idea that we would go from 20 to 34 really is based on, I think, the technical feasibility of what we understand of our platform. There's no magical reason why everybody started at 20. It was a reasonable place to start with where you could demonstrate multiplicity of neoepitopes. But I think understanding and being comfortable with the technology and the process and manufacturing required to deliver longer mRNAs that are still immunogenic, irrespective of where the epitope falls within the chain, based on all the preclinical data that we've done and some refinement of the length of these epitopes, together allow us to push it up to 34.

And at the end of the day, we're playing a numbers game here. It only takes 1 theoretically to elicit the T cell response as long as you get enough T cells, and they're the right kind of T cells, and we've learned that from adoptive T cell transfer studies. So here, we're hoping to stack the deck in the favor of patients such that we're able to elicit not just numerous reactivities but actually reactivities against the epitopes that matter, that may be presented on their cancer cells.

Operator

And our next question comes from Ted Tenthoff with Piper Jaffray.

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Edward Andrew Tenthoff - *Piper Jaffray Companies, Research Division - MD & Senior Research Analyst*

Tal, I want to ask you and kind of put it back to with your clinician experience to kind of put this in perspective. And again, appreciating that this is still very early data and we're still in escalation and even time on follow-up is not fully there. Where do you think these vaccines or your mRNA cancer vaccine, personal cancer vaccine, in combination with KEYTRUDA, would be best used? Is this something where it would go right when they go on KEYTRUDA? Would this be later-stage where you think you might get the best response? And I want to ask you to rectify that with the time that it takes to make these. How feasible is that for really intervening with the cancer patient?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you, Ted. You asked me a couple of questions. So let me start from the end. I think a 50- to 60-day turnaround time, while not ideal and we're continuously looking to improve it, is clearly a good place to start even in the metastatic disease setting where -- because patients can start on pembrolizumab alone while they're waiting for the vaccine. So the quicker, the better. And I think in the future, we're looking to continuously improve on that. But because you can start from pembrolizumab while you're waiting for the vaccine, I think it's reasonable.

You asked me a couple of other questions in terms of where is it best used, so let me make a couple of comments here. First of all, there is a scientific, I think, strong hypothesis why you would want to use such a vaccine in combination with a checkpoint inhibitor. If you look at preclinical data, if you immunize just against a viral antigen, you get a much more robust immune response if you do it in the setting of a PD-1 inhibitor. Now obviously, we wouldn't give somebody KEYTRUDA when we give them a flu shot, but if you would, you would probably get a stronger response. And so I think that the combination with a PD-1 inhibitor makes ultimate sense. And of course, I'm very happy that we're doing this in collaboration with Merck and are able to use pembrolizumab.

In terms of where is it best used. So the truth is that we're going to have to figure this out over time. On purely theoretical grounds, you would expect that in the adjuvant setting, and I don't think this is news, you'd expect that a cancer vaccine should do a better job in the adjuvant setting. And certainly, that should be true for a personalized cancer vaccine because there's minimal residual disease, if any. The patient overall is in a much healthier state, they've been less pretreated. And so especially in a setting where pembrolizumab is already approved, like the adjuvant treatment of melanoma, that makes a lot of sense for me as a place to start.

And that being said, I think we've all been really impressed by the ability of a robust immune system to cure cancer even in a widespread later stage of metastatic disease. And so I wouldn't rule out that we will see benefit in later stages of disease. And I think that our overall plan here is to continue to expand the Phase I trial both in the setting of metastatic disease while we launch this randomized Phase II in the setting of the adjuvant disease.

Edward Andrew Tenthoff - *Piper Jaffray Companies, Research Division - MD & Senior Research Analyst*

Right. That makes a lot of sense, I really appreciate that color. Look forward to more data.

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you, Ted.

Operator

And our first -- next question comes from Salveen Richter with Goldman Sachs.

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Salveen Jaswal Richter - *Goldman Sachs Group Inc., Research Division - VP*

Just with regard to the melanoma portion here. How do you think the relapse rates that you've seen in the Phase -- the Part A and Part B of the study here would translate to Phase II in the context of your trial design?

And then the second question, just your thoughts here about combining CTLA4 in combo with KEYTRUDA in the melanoma study.

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you, Salveen. So let me take these by order. Our assumptions for the randomized Phase II don't really rest on the clinical activity that we've seen here. I think interpreting the clinical activity of this very limited data set across different histologies is really difficult. And I think Ted asked me part of that question as well. The best I can do is refer you to the treating physicians. I think Skip Burris in his comments and other investigators are really interested and curious about what they've seen so far. And I think that's as far as I can go in terms of interpreting these data.

That being said, in terms of setting the setting for the adjuvant assumptions in melanoma, we have recent data from the label of pembrolizumab and there have been studies that led to the approval of these agents in the adjuvant setting. So we know what to expect in terms of a recurrence rate. And what we're going to be doing as this is a relatively small study, we will actually be focusing on patients who've got a higher risk of relapse. So if the label and the Phase IIIs, the recent Phase IIIs were all done in stage 3a, 3b, 3c and 3d, we're actually limiting our patient population to 3c and 3d primarily. We will accept some 3bs if they've had a recent relapse and additional resection. So we're trying to really focus on the patients who are at the greatest remaining risk and need for improvement upon what the PD-1 alone would do.

Your question about CTLA4, I think it's a relevant one. At the current time, we're focusing really on PD-1. I think it's something that we will probably come back to in the future and try to assess. I think the totality of data of immunizing in the context of a PD-1 versus a CTLA4, there's not that much. But my read of the preclinical data would suggest that there's going to be good utility from the combination of PD-1. So while I don't rule out the utility of combining with CTLA4, I think as you start any clinical development path, you have to practically limit the variables in order to figure out whether your intervention is additive.

Operator

And our next question comes from Cory Kasimov with JPMorgan.

Unidentified Analyst

This is (inaudible) for Cory this morning. So just my question is do you have any immunogenicity data for the patients treated in the pembro combo cohort and specifically for the patients who responded to treatment? And if so, what have you seen?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you, [Cory]. At this time, we don't have any data from them. I think one of the learnings from this study is that it requires apheresis to get a more refined data set. And I think the sensitivity of assays that are run just on whole blood is not as high. I think that's one of the learnings we've had here. And so we started by assaying patients on the monotherapy alone just so that we can be sure that what we're seeing is secondary to the effect of the vaccine.

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Unidentified Analyst

Okay, great. And just one more, if I can. Was curious if you could provide a little bit more color on the 2 patients previously exposed to PD-1 or PD-L1 therapy who saw a partial response. How much time had elapsed post the initial treatment? And is it common or rare to see a response to PD-1 monotherapy after initial treatment?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

So without going into the very granular specific of each patient, the time frame is typically weeks to a few months. One of them had progressed on prior atezolizumab and the other had progressed on pembrolizumab. For both, if I recall correctly, the next trial that they came on was our trial, so I'd say it's a fairly recent progression.

In terms of how common, I don't think there's much literature there, but my polling of experts suggest that we don't typically see responses to one checkpoint inhibitor after the failure of another. And I haven't seen any recent studies really that come to mind that people have described this at any level. So it's really hard to know. So all I can cite for you really is my sense of the expert opinion out there.

Operator

And our next question comes from Geoff Meacham with Barclays.

Unidentified Analyst

This is [Scott] on for Geoff. Just thinking as you move into the Phase II trial, can you give us additional context for the high-risk recurrent patient population in melanoma? Should we expect this group would also be high responders to KEYTRUDA alone?

And then the second question is when you think about the timing of moving the asset to the clinic, do you have a sense of the number of planned sites you'll have for the Phase II and how quickly you can get fully enrolled?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you, [Scott]. So starting with your question on response to pembrolizumab alone. The -- I think the expectation is that pembrolizumab would work irrespective of whether you've got a high risk or a low risk. And the problem with the adjuvant setting in terms of defining that is that it's really a population-based effect, so it's hard to know. In other words, in the adjuvant setting, I can't point to a given patient and say they benefited versus they don't. And so the approach we've taken is to stack the deck and focus on those patients who have a higher unmet need by going after those who are known to be at high risk of relapse. And our assumption is that the relative benefit of pembrolizumab, as manifested in the hazard ratio, would stay the same for that population. So that underpins our statistical assumption.

In terms of the number of sites. Look, we're just getting started. This will probably be at least a dozen sites in the U.S. and we're looking at other areas as well. And as these sites come on, you'll see them appropriately listed on clinicaltrials.gov.

Operator

(Operator Instructions) And our next question comes from Alan Carr with Needham & Company.

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Alan Carr - *Needham & Company, LLC, Research Division - Senior Analyst*

Are you going to need more resolution about your neoantigen selection process? And then, if you are, it'd be great if you can talk about that some, and how you select them.

And then also maybe you can comment a bit more about your cursory thoughts on just 1 patient, but your thoughts on the CD8 T cell response rate there, for 10 on 18.

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you, Alan. So selection process. I think what we do is pretty similar to what practically everybody does in this field which is we all start, based on the totality of scientific data available out there, for likelihood of binding. The advantage of an mRNA-based platform is that we design with enough -- we design a neoepitope vaccine that has a mutation in the middle and enough of a flanking sequence on each side of it so that it allows the cells on protozoa machinery to actually pick out what would be the optimal epitope to be presented in the context of an MHC, and as I noted on the call, whether it's Class 1 or Class 2.

So I think our selection process is really trying to weigh -- to give the patient as much opportunity to respond by trying to be as diverse as we can around our MHC's by trying to lock a number that would be predicted to go to Class 2s and by giving the flexibility of a longer sequence that you can do with an mRNA, so that there, we're relying on the patient's own biology to choose the right neoepitope.

In terms of the numbers that you see, a couple of points. So I think 10 out of 18 is a respectable number. I think it's in the ballpark of what anybody else has ever described. And again, I don't expect to necessarily be immunogenic to every epitope. I think the goal is to be immunogenic to enough and hopefully, to those that matter in the context of the patient's T cell's response and ability to recognize their cancer cells. So I'm quite pleased with 10 out of 18. And if that percentage stays that way as we grow the length and able to deliver more neoepitopes, I think it will be good for the patients, or at least I hope so.

The final point which I didn't talk about but which you indirectly allude to is our learning of CD8s versus CD4s. I fully expect this vaccine to be able to generate CD4 T cells. You can see some of that data starting to emerge from the NCI poster. We have not presented any data here. We're still in the process of setting up those assays, CD4 cell assays, for those in the field tend to be trickier than assays for CD8 positive T cells. But if you look at the totality of what we know of our vaccines, especially in the infectious disease side where that level of antibody response likely is associated with CD4 health, although again, I don't have direct data for that, makes me comfortable that we're getting the kind of responses that we're shooting for with our own selection algorithm.

Alan Carr - *Needham & Company, LLC, Research Division - Senior Analyst*

And then a follow-up around 34 mRNAs. Do you -- are you all working to expand beyond that? Or do you think 34 is the right number for now?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

So it is 1 mRNA, it is 34 different epitopes that are all encoded in a single chain. I think for now, I'm happy with that. I'm curious to see the performance. And of course, that is the number that we're taking into a randomized Phase II. So changing in the midst of a randomized Phase II is going to be difficult.

That said, we continue to do research and try to improve on what we have while we're exploring things in the clinic. One of the benefits of having such a flexible sort of information-based modality with mRNA to begin with is that our cycle times in research tend to be very short and the modularity is pretty high. So we continue to explore ways to improve it, while I'm happy with 34 as the number going into the randomized Phase II.

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Operator

And we have a follow-up question from Ted Tenthoff with Piper Jaffray.

Edward Andrew Tenthoff - *Piper Jaffray Companies, Research Division - MD & Senior Research Analyst*

Tal, I was interested by a comment that you made with respect to relapse. And I really do think adding this neoantigen or adding a personalized cancer vaccine, the goal here is not just to get greater immune response but also potentially to kind of, with the KEYTRUDA, extend that durability. So I'm wondering, how do you think about patient characterization early on? And what I'm kind of talking about here is biomarkers, but that's such an overused word. But how do you really start to think about figuring out those patients that may have a better response to the personal cancer vaccine; whether it's some kind of immune marker, whether it's -- or do you think that just by doing this exercise, you're picking the antigens that are going to have the best shot? So I wanted to ask first about kind of are there ways to really kind of get an idea which patients may respond best to this approach?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thanks, Ted. It's a really good question and one that I think we think a lot about. And it's not just us, it's the field in the whole. And if I could use this opportunity to shout out to my colleagues at Merck, I think the team over there that's been working with us has spent a lot of time looking at biomarkers for pembrolizumab, not just PD-L1 but others, and we've been down this journey together with them.

My sense is -- and it's one of the reasons I'm so intensely focused on the adjuvant melanoma setting. I think in that setting, there's a couple of things that are relevant. First, it's melanoma that we know tends to be more responsive, but that's still a large proportion of patients ultimately do not benefit from checkpoint inhibition. And so in the setting of having enough mutations, you're much more likely to have mutations that are highly able to bind and therefore elicit a T cell response. And so it makes sense that, that would be a disease setting to start.

And the other element, while it's not really a biomarker in the traditional sense of something you measure on the tumor, the clinical reality of the adjuvant setting is usually one where the overall burden of disease is low and there hasn't been metastatic spread almost by default, although on occasion, we will resect the single metastatic nodule. And I think that's important because if that is true, then hopefully, there's not much heterogeneity yet or not as much as you would see in the later-stage metastatic setting. And if that is true, then the vaccine that you obtain based on the sequence from a primary or a recently resected lesion should be reflective still of what the cancer is in the micro-metastatic places where you can't find it but you're trying to prevent the relapse. So that's really how I think about it here.

I'm not sure that there's going to be much that will emerge from studying the tumor microenvironment or other biomarkers, although of course, we're looking at that carefully as well.

Edward Andrew Tenthoff - *Piper Jaffray Companies, Research Division - MD & Senior Research Analyst*

I appreciate that extra color, it just was an idea that had come to mind from one of your answers to the other questions, so I appreciate you taking the time.

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Always.

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Operator

Thank you. Ladies and gentlemen, this now concludes our Q&A portion of today's conference. I would now like to turn the call back over to Stéphane Bancel. You may proceed.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Well, thank you, everyone, for your interest and for your time this morning. Have a very wonderful day. Bye.

Operator

Ladies and gentlemen, thank you for attending today's conference. This does conclude the program and you may all disconnect. Everyone, have a great day.

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