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PRESENTATION

Operator

Good morning, my name is Lara, and I will be your conference operator today. At this time, I would like to welcome everyone to the Merck Oncology ESMO Virtual Investor Relations Event Conference Call. (Operator Instructions) Thank you.

I would now like to turn the call over to Peter Dannenbaum, Vice President, Investor Relations. Please go ahead.

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Thank you, Lara, and good morning. Welcome to Merck's 2020 ESMO Investor Call. Today, I'm joined by Dr. Roger Perlmutter, President of Merck Research Labs; Dr. Roy Baynes, Head of Global Clinical Development and Chief Medical Officer; Frank Clyburn, Chief Commercial Officer; and Mike Nally, Chief Marketing Officer.

Before we get started, I would like to remind you that some of the statements that we make during today's call may be considered forward-looking statements within the meaning of the safe harbor provision of the U.S. Private Securities Litigation Reform Act of 1995. Such statements are made based on the current beliefs of Merck's management and are subject to significant risks and uncertainties. If our underlying assumptions prove inaccurate or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements. Our SEC filings, including Item 1A in the 2019 10-K, identify certain risk factors and cautionary statements that could cause the company's actual results to differ materially from those projected in any of our forward-looking statements made this morning. Merck undertakes no obligation to publicly update any forward-looking statements. Our SEC filings are posted on merck.com.

Roger will begin today's session with a slide presentation, which has been posted to our website, and then we'll follow with Q&A. So with that, I'd like to turn the call over to Roger.

Roger M. Perlmutter - Merck Research Laboratories - President

Thank you very much, Peter. I hope everyone can hear me. Good morning.

So to begin, we have our forward-looking statement, which Peter has already covered. And then I'd like to try and place the results that we've presented at ESMO in some context for you. And thereafter, we'll take your questions.

So as everyone knows, this has been a long odyssey for us as we have pursued the introduction of immuno-oncology into the routine treatment of malignant disease. This slide shows you our approach. And if we start at the right-hand side, part of our approach has been to identify those patients who are most likely to benefit using biomarkers, initially, of course, with the PD-L1 biomarker for KEYTRUDA, and thereafter with MSI-high tumor mutational burden and a variety of other biomarkers that we've used for other programs that I will have a chance to comment on. We've also advanced our pipeline with strategic collaborations, and we'll talk about a number of those, while at the same time, emphasizing those things that we've generated internally like KEYTRUDA.

We've broadly explored combinations, and the combination data are some of the most interesting and important that we'll have a chance to cover. Keep in mind that we started out initially trying to understand exactly how well KEYTRUDA could work in a whole variety of different tumors as monotherapy. And we use that information from monotherapy to establish the benefit that inures in combination, for example, with KEYNOTE-189 in combination with chemotherapy in non-small cell lung cancer. And the results have been, as everyone knows, extremely important. All of this speaks to the fact that KEYTRUDA is foundational in the treatment of malignant disease.

Now those combinations, of course, have come to occupy a substantial amount of what we are doing in our clinical research, and it is a very large clinical research program, as you know, right now on the order of 1,300 ongoing clinical trials, 900 of which are combination trials and 90 of which are registrational. That is, could permit registration, assuming that the data work well. I should also point out that about 110 of those trials are looking at quite early-stage disease, adjuvant and neoadjuvant therapy. And of course, we have had interesting results in those early phase studies already and have even some long-term data to show you with respect to adjuvant treatment in melanoma.

So if you look at the foundation at KEYTRUDA, KEYTRUDA now has more than 30 indications in the United States. It is the first truly broad-spectrum antineoplastic agent ever introduced into clinical practice. It has benefited, of course, from combinations with a whole variety of different chemotherapeutic regimens. And it is also being explored in combination with our partnered molecules, LENVIMA and LYNPARZA, and data from those kinds of studies are accruing. In addition, we've added other new collaborations, most recently our Seattle Genetics collaboration.

But during this ESMO, we had a chance to talk about some of our newer molecules that have come from our own research. For example, vibostolimab, the anti-TIGIT molecule and our ILT4 program, which I'll briefly highlight. So we're engaged in a whole variety of different studies that build upon the foundation of KEYTRUDA to make it an even more effective antineoplastic therapy.

So what happened at ESMO? Well, at ESMO, we presented new Phase III data for KEYTRUDA in first-line esophageal cancer based on the KEYNOTE-590 study, which we'll talk a bit about the results of that. We also had combination data for KEYTRUDA plus LENVIMA, as I've mentioned, and had a chance to present the overall survival data for LYNPARZA in metastatic castrate-resistant prostate cancer from the PROfound study.

The long-term benefits data are worth lingering on, and I'll just show those slides for a number of the studies. But certainly, with respect to KEYTRUDA in non-small cell lung cancer and the PD-L1 high population, based on KEYNOTE-024, our initial landmark study, are quite remarkable; similarly for adjuvant melanoma and head and neck cancer data from KEYNOTE-048 in combination with chemotherapy; and as well the long-term, progression-free survival data for the use of LYNPARZA in ovarian cancer based on SOLO-1; and then, of course, the new mechanisms, which -- about which I've already spoken a little bit.

So let's take a look at the KEYNOTE-590 data. And what you're seeing here is the overall survival data that were presented, showing that KEYTRUDA in combination with chemotherapy reduced the risk of death by about 27% compared to chemotherapy as a first-line treatment for patients with metastatic esophageal cancer, which of course, is a devastating disease. And what I guess I would emphasize here is the breadth of this response, because those -- the treatment effect of KEYTRUDA was true with respect to overall response rate, progression-free survival and overall survival and was superior compared to chemotherapy irrespective of the histology of the esophageal malignancy and irrespective of PD-L1 expression status. So an extremely broad-based set of data there, extremely important results in this devastating disease.

We also, of course, had the opportunity to talk about what is becoming, unfortunately, a new frontier, and that is what do we use to treat patients who have failed to progress on KEYTRUDA or other PD-1/PD-L1-directed therapy. We've done quite a lot of work to rigorously define that population, recognizing that some patients respond late to KEYTRUDA therapy, and that some patients who progress after KEYTRUDA therapy, particularly in certain especially responsive settings like melanoma, some people who progress will respond upon retreatment after -- if they've gone into a hiatus. So it's important to rigorously define these individuals who have failed PD-1/PD-L1 therapy.

But in that population, in the melanoma setting, LENVIMA in combination with KEYTRUDA, showed really impressive overall responses based on blinded central review. The overall response rate was over 21% by RECIST version 1.1. And in the certain subpopulations, it was even better with a nearly 14-month median overall survival.

What I'm saying is that we believe we are beginning to see opportunities to rescue patients who progressed after having PD-1-directed therapy, even KEYTRUDA, to rescue them using combinations with KEYTRUDA. And that's an important result and one that will become more important over time because, of course, so many patients are receiving KEYTRUDA.

The long-term survival data are really extremely important. And if you look at non-small cell lung cancer, just as an example, and I mentioned this before, the survival rate for patients with non-small cell lung cancer in the KEYNOTE-024 study, which, of course, is the PD-L1 high, with tumor proportions greater than 50% population, at 5 years, so this is a 5-year data, and the response rate has doubled. The duration of response was 5x longer with KEYTRUDA monotherapy than with chemotherapy after 5 years. So there shouldn't be much question about the durability of KEYTRUDA therapy in this context. It's quite extraordinary.

And as I've mentioned to you before, I hear from many thoracic oncologists, who are now seeing patients in follow-up, something they've never seen before. Because as we know, the survival for individuals with advanced non-small cell lung cancer prior to the introduction of KEYTRUDA was measured in months.

If we look at head and neck cancer, based on the long-term follow-up of KEYNOTE-048, improved overall survival versus an -- the extreme regimen, a very potent regimen, chemotherapeutic regimen. And you can see that the overall survival curves, the Kaplan-Meier curves, differ substantially.

And similarly, in the 3-year follow-up, looking at metastasis-free survival on the graph, so alive and metastasis free, very impressive data in the adjuvant setting in KEYNOTE-054 in melanoma, demonstrating the early treatment effect. So these are really (inaudible) results and something quite meaningful for a very, very large number of cancer patients.

We also had the opportunity to look at long-term follow-up data for LYNPARZA, showing the overall survival benefit in BRCA1/2 mutated or ATM-mutated metastatic castrate-resistant prostate cancer and progression-free survival in BRCA-mutated advanced ovarian cancer based on the SOLO-1 data. And again, there's no ambiguity to these Kaplan-Meier curves. It's really an extremely impressive result.

I have to say with LYNPARZA, the stability of these patients, their ability to stay on treatment for years is quite remarkable. And that in a disease process that is, I think most of you know, in ovarian cancer in these patients, that's a very responsive tumor, but relapses occur early and people cycle through many, many therapies before succumbing. The fact that you can maintain a progression-free survival, median progression-free survival for more -- almost 6 years, -- I mean, sorry, almost 5 years, 56 months, is an amazing thing and reflects the ability in this population of ovarian cancer patients the ability of LYNPARZA to have this stabilizing effect. So really quite extraordinary long-term data. And of course, the data in castration-resistant prostate cancer, extremely important for this subset of patients.

Now we also had the opportunity, as I mentioned, to introduce new information with respect to vibostolimab, which is our TIGIT-directed antibody. This is first time data, showing you here the waterfall plot. The vibostolimab used in combination with KEYTRUDA showed compelling response rates in patients who are naive. And it also showed responses in individuals who had rigorously progressed. We are moving vibostolimab into Phase III in 2021 and performing a variety of different exploratory studies to detect other signals. So we're optimistic that this combination could prove to be effective. We'll have more to say about that later.

But we also had the opportunity to test another monoclonal antibody, this directed against ILT4. Its MK-4830. And we're presenting here for the first time initial efficacy data from Phase I dose escalation studies.

And what's interesting here is that ILT4, first of all, is the antibody 4830 directed against ILT4, is directed against the tumor microenvironment. This is not an antibody that interacts with T cells to an appreciable extent but affects the ability of the microenvironment to control the immune response. And because we and others believe there are suppressive elements in the microenvironment, it made sense to try and pursue that. We did that. The preliminary efficacy data show an overall response rate of 24% in patients who are receiving 4830 in combination with KEYTRUDA. And we can exclude the KEYTRUDA-only effect in a variety of ways, but I've mentioned one, and that is in patients who have rigorously progressed on prior PD-1 therapy, including KEYTRUDA, there were 5 responses. I wouldn't say that we're always going to see 45% response rates in that population, but it indicates that once again, the combination of these 2 therapies can rescue responses in individuals who rigorously fail KEYTRUDA. And that's an important observation and something that we're going to have an opportunity to pursue in much, much more detail. Obviously, umbrella studies designed to detect additional signals with MK-4830 are underway.

And lastly, let me turn to another program, which is our HIF-2 alpha inhibitor, MK-6482, taking advantage of important work that defines the mechanism of activation of malignancy in renal cell carcinoma and in a variety of other different tumor types. Individuals who have mutations in HIF-2 alpha, who are -- who inherit those mutations have a syndrome called von Hippel-Lindau syndrome, which is associated with clear cell renal carcinoma, and also a whole variety of nonrenal cell carcinoma malignancies and benign tumors as well.

And so you can see many of those that are on the right-hand side of the panel, and most of you are familiar with von Hippel-Lindau, we had the opportunity to present additional data on our study of MK-6482 in treatment-naive patients with von Hippel-Lindau-associated renal cell carcinoma with a confirmed overall response rate of 36% and unconfirmed partial responses in a number of other patients. These responses tend to occur fairly late, but they appear to be quite durable. The median duration of response has not been reached. And more than 90% of patients remain on study therapy.

Interestingly, and speaking to the fact that the HIF-2 alpha mutation, in fact, is a driver mutation for both the benign and the malignant lesions. If you instead focus on other lesions, with pancreatic lesions, for example, or hemangioblastomas in the central nervous system, response rates are also quite high. And in the retina, the vast majority, nearly, 94% of patients had -- were either improved or stable with respect to their retinal lesions, hemangioblastomas and others. So that's -- those are really important results and suggest that MK-6482 could provide the first new therapy for patients with von Hippel-Lindau syndrome, who typically undergo multiple surgical excisions in order to treat the number of different tumors that they develop.

That is an example, of course, of an important business development activity that we pursued. We had discussed the work of Peloton with them for a long period of time, watching as they went through first one and then another compound. And when the opportunity presented itself, we were able to acquire Peloton and are now using MK-6482 in a variety of different settings because we think it will be important as a new tool to treat malignant disease.

And we're doing exactly the same kinds of things with our (inaudible) inhibitor acquired from ArQule, with the new programs from Seattle Genetics just announced as well as our collaboration with them on EV and with a variety of other earlier stage programs, including a coxsackievirus A21 virus as an oncolytic virus to be used in combination with KEYTRUDA that also has monotherapy activity.

So these are important collaborations for us. And they emphasize the strength, both of our internal research program with KEYTRUDA as the foundation and as well our ability to advance other programs once they become promising, that the broad oncology community has been able to develop. So with that summary of the work that's been presented at ESMO, we'll take your questions. Thank you very much.

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Thank you, Roger. Lara, if you could start the Q&A process, please. (Operator Instructions)

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Your first question will come from the line of Terence Flynn from Goldman Sachs.

Terence C. Flynn - *Goldman Sachs Group, Inc., Research Division - MD*

Great. Maybe just 2 for me. Roger, based on your presentation, it sounds like, obviously, a big push is in patients that progressed on PD-1 or PD-L1 inhibitor. Just anything common that you guys are finding about those patients with respect to either pathways or underlying biology that you could share at this point? I know you've done a lot of work there.

And then with respect to your anti-TIGIT antibody, is there any reason why this would only be active in lung cancer? Is there something special about lung cancer? Or would you expect this to be more broadly active based on what you're seeing thus far?

Roger M. Perlmutter - *Merck Research Laboratories - President*

Thanks for the questions. I -- and I'll let Roy respond to this as well because he'll have some other thoughts.

But first of all, I wish I could say that we understand exactly why individuals progress after treatment with KEYTRUDA or other PD-1 or PD-L1 therapy. And the answer is that we don't. And the -- to be honest, part of the reason why we don't is we still don't understand why some people respond and some people don't to KEYTRUDA therapy. So I've talked before about the heterogeneity of the responding population and why it might be that knowing that KEYTRUDA reveals the preexisting immunity directed against the tumor that's present in a substantial fraction of cancer patients, more in some tumors than in others. Why? We don't know. We still can't describe what the antigens are that the tumors -- in the tumors that are being recognized. We have a few examples, but very few. What we can say is that there's no common antigen even for a single tumor type.

And we don't know why it is that a situation that seemed to have been in balance for a period of time, tumor, growing, response, preventing tumor growth, goes out of balance and why it is that we can recover those T cells. Some people have described them as being in an exhausted state using KEYTRUDA.

So similarly, we don't understand what happens when, once again, KEYTRUDA does not seem to rescue that immune response. We're hopeful that, that immune response can still be rescued and that in some cases, and vibostolimab might be an example, we can make that work. And there's no reason to expect that, that would only be true in a lung cancer setting. And indeed, we have data in other tumor settings and a variety of signal studies -- signal identification studies going underway. So that gives us a sense of that, and we're optimistic about those studies.

Roy, what did I miss?

Roy D. Baynes - *Merck & Co., Inc. - Chief Medical Officer*

Well, Roger, I think you answered that perfectly. I would just say in the primary resistant stage, we are starting to have an approach to that. You can think about cancers in many different ways. You can think of them as sort of histologically being predictive or you can think about tumor-infiltrating lymphocytes.

We actually had a very nice paper in Science in 2018 where we basically looked at lung cancer patients arrayed, or partly cancer patients arrayed by, if you will, tumor mutational burden on the y-axis and degree of tumor inflammation on the x-axis, which divides the population logically into quadrants. And interestingly, when you put additional biomarkers on top of that, you do find suggestions of what combinations might be meaningful. For example, highly inflamed, nonmutated tumors often have an angiogenesis signal. Highly inflamed, but -- and high mutational burden oftentimes have other checkpoint signaling or costimulatory signaling. If you look at the group that's noninflamed and nonmutated, those typically show

evidence of resistance biology, unique genetic expressions which may portend resistance. And then in the non-inflamed and highly mutated, we often see a proliferative signal. You might think that something like chemoradiation may be very effective there.

So there are some clues, and there's been 1 or 2 publications where, for example, melanoma patients who became resistant might have had some amplification or mutation of the Janus kinase pathway. But we're pretty early in this journey. As Roger said, we really don't understand this terribly well.

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Roger, I believe there is a second question on TIGIT.

Roger M. Perlmutter - Merck Research Laboratories - President

Well, I'm sorry, I thought I had answered that. That there, we are -- it does work in other tumor types and in signal finding studies, we're seeing that.

Operator

Your next question will come from the line of Navin Jacob from UBS.

Navin Cyriac Jacob - UBS Investment Bank, Research Division - Equity Research Analyst of Specialty Pharmaceuticals and Large Cap Pharmaceutical

Libtayo showed this pretty compelling data in first-line, non-small cell, over 50% expressers. That space is starting to become relatively competitive. Wondering if you could remind us of the various means that you will use to defend the over 50%. And just the broader first-line, non-small cell space, whether that's with your own TIGIT or other combinations down the road?

And then on MK-6482, will this drug only be developed for VHL-associated disease? Or do you see activity beyond that? And specifically, in the first-line renal cell carcinoma space, can you provide some clarity on your development plans with 6482 there?

And then finally, on 4830, just wondering if this type of asset, tumor microenvironment product, is ideally suited for the post PD-1 therapy space. Or do you think it has any possibility of moving up in the line of therapy?

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Thank you, Navin. Why don't we start with the clinical question. So Roger and Roy on 6482 and 4830. And a view on -- in first-line lung on Libtayo, that would be helpful as well. And then we'll get to Frank with a little bit of a commercial take.

Roger M. Perlmutter - Merck Research Laboratories - President

Right. So there are 3 questions, and I'll just -- it's hard to know how to break these out exactly.

But first of all, with respect to the lung space, we are, of course, expecting, it's understandable, that now that we've established the broad utility of KEYTRUDA, there will be many others, and there have been many others, that will be pursuing PD-1 or PD-L1 intervention in that space. I think our data speak for themselves that the long-term outcomes are extraordinary and our expectation is that others will have to, over time, try to surmount that wall of data that supports the use of KEYTRUDA. Not saying that over time, other things won't be found, and indeed, we spend our time looking for what happens afterwards. KEYTRUDA provides enormous benefit, but we need to do still more.

6482 for von Hippel-Lindau, clearly, the vast majority, over 90% of spontaneous renal cell carcinomas have HIF-2 alpha mutations. We've already demonstrated that 6482 is active in the setting of spontaneous renal cell carcinoma. And that is the registration program, of course. von Hippel-Lindau is an especially salient observation, but the broad implication is that HIF-2 alpha is a mechanism that controls cell growth, certainly in the renal cell setting, but also in other settings.

And for 4830, again, the combination data, I think, are compelling. And the idea is that, that should be useful in a whole variety of different settings.

Roy, you can add some comments. And then I think we'd probably like to hear from Frank about the lung cancer environment.

Roy D. Baynes - Merck & Co., Inc. - Chief Medical Officer

Sure. So thanks, Roger. In the lung cancer environment, I think, firstly, to just state the obvious, we do have a significant first-mover advantage here. We've just shown 5-year survival data. These new data that you saw from a competitor are really their first presentation. So the track record of KEYTRUDA is obviously very, very well established.

I think it's also important as we look at these trials -- and we'll learn a lot more as they get published. Just make sure that the populations are comparable. I'll just give you one obvious quick example. The Libtayo study excluded nonsmokers. Now we know that nonsmokers are, in fact, more -- or less responsive than smokers. So this is obviously a population that was pretty much enriched for an outcome. And again, we do have the 5-year data, which Roger has already spoken to, and extremely compelling. I have nothing to add on the question of the other 2 agents. Thanks, Roger.

Franklin K. Clyburn - Merck & Co., Inc. - Chief Commercial Officer & Executive VP

Yes. Navin, this is Frank. And I just had a couple of points that Roy mentioned. The 5-year overall survival data is really important to us. In most markets now around the world, especially in the PD-L1 high population, KEYTRUDA has established itself as a standard of care based off of KEYNOTE-024 and KEYNOTE-042. And remember, we have 5 trials of overall survival in non-small cell lung cancer across both squamous and nonsquamous histology.

The other thing I would add, in addition to just the PD-L1 high population, we continue to see very strong performance across all patients based off of not only our monotherapy, but also our combinations of KEYNOTE-189 and 407. So as Roger mentioned, there's a number of new competitors that have come into the non-small cell lung cancer space. What we're seeing evolve early on in the U.S. market is while we are seeing some use from some competitive regimens, our overall share has remained steady. And we're still seeing approximately 8 out of 10 patients being started on a KEYTRUDA regimen, and we feel very confident about our position in non-small cell lung cancer.

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Great. Thank you all. Lara, before we get to the next question, I know some people are having trouble dialing in to ask questions. The international number works. Now I'll quickly give you that number. It's (469) 886-1947 and the ID is 7114498. Thank you.

Operator

(Operator Instructions) Your next question will come from the line of Louise Chen from Cantor.

Louise Alesandra Chen - Cantor Fitzgerald & Co., Research Division - Senior Research Analyst & MD

So my first question is on KEYNOTE-522. If it's approved as a regimen, where do you see it fitting in for triple-negative breast cancer, given some competition here? And how will it be supported by KEYNOTE-355 and your other triple-negative breast cancer programs?

And then similar question for KEYTRUDA plus anti-TIGIT regimen. If it's approved, where do you see it fitting in, given competition?

And what's the unmet need for an IO-IO sparing regimen?

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Roger or Roy?

Roger M. Perlmutter - Merck Research Laboratories - President

IO-IO sparing regimen, okay, I'm not sure what that means exactly, Louise. But on the others, let me just...

Louise Alesandra Chen - Cantor Fitzgerald & Co., Research Division - Senior Research Analyst & MD

I'm sorry, I meant a chemo-sparing regimen, an IO-IO chemo-sparing regimen.

Roger M. Perlmutter - Merck Research Laboratories - President

Okay. Got it. That, now I understand. So the triple-negative breast cancer population is an important one, and there's a lot of really important nuance to this, and I'm going to let Roy speak to KEYNOTE-355 and 522, the neoadjuvant adjuvant study, which, of course, is a study that's, well, both still going on.

And I think that just at the high end, what are we trying to do here to address the last question? What we're trying to do is to improve the benefit-risk profile for patients generally with cancer. And we started out, this obviously began decades ago with cytotoxic chemotherapy, which provided some benefit, but not very much, titrating patients to the limits of toxicity. There were occasional cures in some settings and particularly in pediatric malignancies. But in general, those therapies did not perform terribly well. We had decades of combination therapies, additional therapies. And then, of course, immuno-oncology, which revolutionized the treatment of cancer, particularly, as I say, with KEYTRUDA and the breadth of its indications.

KEYTRUDA is a terrific drug. It's not perfect either. There are adverse experiences associated with it. And of course, people do eventually relapse, not all, but some do. There are some very long-term durable responses. And so the goal is to come up with still better therapies, and that could be achieved with combinations. Many of the combinations, particularly with vibostolimab, with 4830, the adverse experience profile is not much changed by the combination. And so in that setting, I think you can imagine ending up with these particular tumor types in which we have regimens that have a much improved benefit-risk profile. And going forward, we'd like to see that get better still. I mean that seems, I think, pretty straightforward.

But Roy, you might want to talk a little bit about triple-negative breast cancer.

Roy D. Baynes - Merck & Co., Inc. - Chief Medical Officer

Sure. Thanks, Roger. So the questions, as I understood them were, firstly, where would our KEYNOTE-522 study fit in? Well, perhaps I should just start off and say that this is the largest neoadjuvant/adjuvant trial conducted. We have presented the results of interim analyses, where we showed a highly statistically significant and clinically meaningful improvement in pathologic complete response rate. This is really quite well validated as a surrogate marker for a favorable outcome in such patients. And on the basis of that, we have submitted the data for regulatory review.

I would say that the information from other sponsors has been a little bit confusing. One trial showed -- that was presented at ESMO showed a benefit in terms of path CR, much smaller study and really no EFS data. You should recall that our data at -- based on interim analysis #2, did show directionally favorable event-free survival.

In addition, other trials in this setting have actually failed from a competitor. And so I think that really KEYNOTE-522 really sets the bar. And this trial will obviously continue to provide readouts over time. We do believe, ultimately, that in the fullness of time, survival benefit is likely.

Where does KEYNOTE-355 fit in? So KEYNOTE-355 really looks at the combination of chemotherapy plus PD-1 antibody, our PD-1 antibody, in the frontline treatment of metastatic triple-negative breast cancer. I should point out that in our trial, in fact, all chemotherapies were allowed. Physicians selected the chemotherapy. These were either taxane-based or platinum-based. And indeed, both taxanes were allowed. We have presented already the data here that in the PD-L1-selected population, there is a highly statistically significant and clinically meaningful improvement in progression-free survival. We have not yet communicated the overall survival on the study. But as you know, PFS is an approvable end point in this disease. And importantly, there's consistency between the various chemotherapy regimens. We will be presenting those data in more detail later in the year.

I would just say that we certainly, in the neoadjuvant setting, have shown very clearly that the platinum-based chemotherapy really does set the bar. If you look at our pathologic CR rate in 522 on the basis of a platinum regimen, because 522 was platinum-based, we have the highest ever reported path CR rates. And indeed, the path CR rate for the chemotherapy itself is also quite appreciable, in fact, surpassing that of competitive data based upon taxane. So again, we do believe that platinum plus a PD-1 does set the bar by which neoadjuvant regimens should be assessed. So we actually feel very good about the data from KEYNOTE-522 and KEYNOTE-355 and really do believe that they will represent important practice-changing data.

Roger M. Perlmutter - Merck Research Laboratories - President

And if I could, Louise, just -- thank you, Roy. I would mention for KEYNOTE-522, just anecdotally, this is a regimen that Roy and I get a lot of calls about, because for a young woman diagnosed with triple-negative breast cancer, where the goal is cure or long-term survival, a neoadjuvant/adjuvant regimen is typically selected. And the 522 data, as Roy says, are the best data that exist. Now that's not an approved regimen, but people are extremely interested in it in the practicing community, I think that's fair to say.

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

And Roger and Roy, on the IO chemo-sparing question.

Roger M. Perlmutter - Merck Research Laboratories - President

Yes. I thought I answered that one.

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Okay. My bad. Seamus Fernandez e-mailed a couple of questions from Guggenheim. The first, I believe, would be a Roy question.

Can you comment on the opportunity for LIV-1, and the opportunity you see for this drug alone and in combination with KEYTRUDA? And then further, any comments on the PADCEV data and approval? That's the first question.

Roy D. Baynes - Merck & Co., Inc. - Chief Medical Officer

Okay. Well, I'll certainly take a shot at it, and Roger may have additional comments.

I think the whole area of antibody-drug conjugates has been around for quite a while. The big idea here was, could you open a therapeutic window by selectively delivering a payload of usually chemotherapy-type warheads directly to the tumor? And for a long time, these -- this promise was really hard to realize. However, with the advent of certain novel antigens having been identified and employed in the delivery of the ADC, we are starting to see some pretty meaningful results.

So for example, if we look at LIV-1, LIV-1 is a very widely expressed antigen in a number of different cancers. And importantly, if we look at the expression, this is in many, many different tumor types, and we do believe that as monotherapy, this will be an important target to pursue. We also have already presented some data in combination with pembrolizumab. These were presented at the San Antonio Breast Cancer Conference previously, showing very meaningful response rates.

In terms of the PADCEV molecule, this has obviously been shown to be very active as a salvage therapy, as monotherapy. And you're probably remembering the data from ESMO last year where the combination with KEYTRUDA showed really quite remarkable response rates. And we are collaborating with Seattle Genetics to -- and Astellas to deploy a pretty broad array of clinical trials where we do believe the combination of PADCEV plus pembrolizumab has the potential to be transformative in the setting of urothelial malignancy.

Roger, I don't know if you want to add anything else.

Roger M. Perlmutter - Merck Research Laboratories - President

No, I think that's perfect. The only thing I would say is, Seamus, that as you'll recall, in this long history of trying to improve the therapeutic index of chemotherapy, it actually started out with toxins. The original antibody-drug conjugates were conjugates of monoclonal antibodies with things like ricin, and that evolved to more traditional chemotherapeutics. But the search was always for a tumor-specific antigen to really broaden the therapeutic window. And the field labored with this, trying to find an antigen that was uniquely expressed on the tumor and no place else and how could we make that work. And I think that in addition to improvements in linker and the selection of payload, the recognition that broadly expressed antigens like LIV-1, like netrin, like other things that have been explored -- and I give Seattle Genetics a lot of credit for their explorations here. It turned out to be good targets for these conjugated therapies and do open the therapeutic window. There's still, of course, adverse experiences related to the intrinsic toxicity of the chemotherapeutic payload. But nevertheless, it turns out to be pretty exciting.

And the other thing that's quite exciting, of course, is that there is a phenomenon of immunogenic cell death, such that the death of tumor cells in this context seems to stimulate immune responses and does so to an even greater extent in the presence of KEYTRUDA, as was demonstrated with urothelial malignancy data that -- with PADCEV that we presented at ESMO last year.

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Great. Thank you, Roger. Well, then Seamus' second question is concerning renal cell carcinoma. He says, CheckMate 9ER showed a surprisingly overall profile, particularly on tolerability. What's Merck's current market share? And how do you see the market evolving in the next couple of years? And what are you doing to manage the tolerability questions around LENVIMA combination.

So perhaps we start with Roy and Roger on the clinical aspect of the question, then turn it to Frank for some of the market questions.

Roger M. Perlmutter - Merck Research Laboratories - President

I'll let Roy take this, but I would say tolerability is not our problem. So Roy, you can take that one.

Roy D. Baynes - Merck & Co., Inc. - Chief Medical Officer

Yes, I completely agree, Roger. I think that, again, we do have the privilege of being a first mover here. And so while the cabo data looks broadly similar to the pembro, axi data, remember, 426 has a lot longer follow-up. And these results really are quite durable and really do portend meaningful outcomes advantage for patients.

Much was made of CR rates. In fact, they were misquoted by the discussant. The CR rates are actually broadly similar, particularly with the updated data.

Cabo is actually recognized as a fairly toxic regimen. And I think you have to recognize that the dose here was quite reduced. It was not dosed at full dose. It was dosed at 40 milligrams.

Again, the adverse event profile of pembro, axi is actually well recognized by the practicing community and well managed. We haven't yet read out the pembro, lenva data, and we look forward to that readout.

I would just also again encourage that look carefully at patient selection because not all these trials can be compared directly. For example, there is a substantially smaller portion of good risk candidates in the cabo, nivo data presented. And you'll recall, that's an area where, indeed, responses have been more difficult to measure. So they actually have a trial, which is relatively enriched for poor risk patients who tend to be much more responsive to these therapies. So again, these trials are not created equal. They have to be looked at with some discernment.

Roger, I don't know if you want to add anything.

Roger M. Perlmutter - Merck Research Laboratories - President

No, I think that's exactly right. In terms of the market, though, Frank, maybe you would like to talk about renal cell carcinoma.

Franklin K. Clyburn - Merck & Co., Inc. - Chief Commercial Officer & Executive VP

Sure. Thanks, Roger. And just want to echo a couple of things, and I think it's important for us to look back that we received approval in April 2019 for RCC. And what we've seen in the marketplace -- and I'll speak to the U.S. but also outside the U.S. here for a second. We have to remember that KEYTRUDA, Inlyta is approved across all 3 IMDC risk categories. We saw a very strong and rapid uptake across patients with favorable, intermediate and poor risk patients. I think it's important to reinforce that the data that we have around overall survival, progression-free survival and strong response rates has resonated very well in the marketplace.

I've seen some data that -- the most recent data set I've seen is in July of this year. And the regimen of KEYTRUDA and Inlyta now has about a 47% share. So we have a market-leading share in the first-line setting. It's important to note that the IO class has about 80% penetration, so about 20% is still CKI monotherapy, which I think offers some additional opportunities. But we feel very good about our first-mover advantage as well as our position in the market.

The only thing I'll also add is, I just saw some data from Germany last night, and we are seeing very strong uptake of the combination of KEYTRUDA and Inlyta in the German market, which I think is a very good, strong signal for ex U.S. opportunity with this important regimen for patients.

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Great. Thank you, Frank. Lara, before we move back to the queue, Andrew Baum from Citi has asked a question with respect to MK-4830, our ILT4. He asked why does CT.gov show it on hold.

And I can answer that, actually. The hold is not due to safety or efficacy. We anticipate that hold to be lifted and the trial to resume as normal in the very near future.

So Lara, if you could go back to the queue, please?

Roger M. Perlmutter - Merck Research Laboratories - President

Just a second. I mean with regard to that question, it's our own procedural hold, just having to do with operations. It's not -- has nothing to do with the behavior of the drug. That's the response to Andrew.

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Okay. Thank you, Roger.

Operator

(Operator Instructions) Your next question will come from the line of Daina Graybosch from SVB Leerink.

Daina Michelle Graybosch - SVB Leerink LLC, Research Division - MD & Senior Research Analyst

Awesome. Two from me. One, we saw, I guess exciting for IO, the early-stage success of the nivolumab combination in adjuvant esophageal. And in that discussion and others at ESMO, I noticed a lot of conversation around using ctDNA MRD to similarly enrich for high-risk, early-stage populations to get successes. And I wonder how you guys are thinking about using that in your trials for KEYTRUDA and others going forward, especially maybe because you've seen some failures, like TECENTRIQ failed in bladder earlier.

And then the second question is, the lenvatinib data was really pretty exciting, and you got some rich discussions at ESMO. But some just focused on the contribution of parts of some speculation that lenvatinib could be bringing this efficacy alone. I wonder if you could talk to why you think the combo is synergistic with pembrolizumab.

Roger M. Perlmutter - Merck Research Laboratories - President

Thanks very much for the questions. I'll let Roy take both of them because I think he has a deeper understanding of the data. Roy?

Roy D. Baynes - Merck & Co., Inc. - Chief Medical Officer

Sure. So we agree that the nivo adjuvant data were really quite interesting. And I think the whole question here is, and I think the presenter made this point, that this is actually really a first in this area. Part of the challenge is the paradigm for treating these diseases varies quite a lot globally. In some jurisdictions, there's more of an emphasis on chemoradiation. In other, there's more of an emphasis on chemo. And the fact that there were some proportion of gastric cancer involved complicates the story yet further.

So despite that, it was a fairly positive trial and obviously exciting for patients, and we'll have to see how the marketplace adopts this type of strategy. We have a bit of a different strategy. We have 2 adjuvant trials ongoing, and they are tailored to the specific anatomies and the specific treatment paradigms.

In terms of ctDNA enrichment, it's obviously an evolving and an exciting area. Circulating DNA does lend itself to some interesting scientific questions. Just in broad buckets, there's the question of, can you select treatments based upon it? Can you monitor treatments based upon it? Can you indeed use clearance of ctDNA as a surrogate for response? And is there any possibility that this could indeed become a surrogate end point?

So it's an important area. It's one that is quite early in the journey, and there's a lot of interest in pursuing it. And we, too, are pursuing the liquid biopsy, if you will, with a high degree of enthusiasm.

In terms of the lenvatinib question, yes, we agree that the data for lenvatinib were exciting. When you talk about synergy, that's a difficult concept. Synergy is something which is well studied in the test tube with antimicrobial agents. But when we talk about clinical trials, synergy is always a relatively difficult concept to advance. And so really, the bigger question is, do you get some increased activity related to the combination versus either alone? And I would say that we do have broad data around what the prospects for lenvatinib alone are in the tumors that we are studying. And it has been our findings from Phase II that the combination of lenvatinib plus pembrolizumab is extraordinarily active. And certainly, we have been very encouraged by the Phase II data that we've seen.

And also, as you saw at the meeting, this also refers to the circumstance where patients have failed a PD-1 or PD-L1 antibody, which is, as Roger mentioned, unfortunately, an increasing population with clearly unmet need in that there is no defined therapy in this population. So we're very encouraged by the findings, and we do believe that the contribution of components is well understood.

Operator

Your next question will come from the line of Steve Scala from Cowen.

Stephen Michael Scala - Cowen and Company, LLC, Research Division - MD & Senior Research Analyst

Two questions, both on TIGIT. First, does Merck place any stock in the early data suggesting potential efficacy in the PD-L1 low, non-small cell lung cancer population? So for instance, are you confident it is a real finding? Or is it more likely a signal, not uncommon in small studies?

And then secondly and stepping back. Roger, as you think about the development of immune targeting agents over the last few decades, how do you view the data for TIGIT thus far? I appreciate that it's early, but does it simply cross some minimum bar to make it good enough to pursue? Is it one of the most exciting targets ever? Or is it something in between?

Roger M. Perlmutter - Merck Research Laboratories - President

Well, Steve, first of all, I would say with respect to our vibostolimab data in the PD-L1 low, that is those individuals who are 1% or less, those data are real. I don't think that there's any ambiguity about it.

The question is, what -- can we provide a numerical estimate for how good the response is? I think the fact that we see responses there, I think, is reassuring in terms of the contribution of vibostolimab to the total response picture that we see in combination. And this gets back to the additivity, the degree of additivity. Synergy is too much to hope for, but the degree of additivity that one sees with new agents added to KEYTRUDA, we're very confident we're seeing some additivity there. The magnitude of that additivity is what will need to be addressed in much larger studies, but we're optimistic at this point. And that gets to the question of how do we place this in the context of other agents.

And the reality is that there -- it has been difficult, even with agents with documented single-agent activity, for example, with ipilimumab directed against CTLA-4, to show that the combination actually is better than a PD-1 directed therapy, in that case, nivolumab plus ipilimumab together. A variety of studies have been done comparing that with ipilimumab alone, showing that nivolumab added something. But the flip side of that, well, that still hasn't been adequately tested. And we're testing that with KEYTRUDA and ipilimumab and, of course, testing it with our own CTLA-4 directed antibody, MK-1308, which we haven't talked about much here. But we believe there are some opportunities there, and they -- ultimately, we're hopeful that with 1308 anyway, we'll be able to see some activity, and similarly with vibostolimab.

The answer to the question of how good is it, is -- well, we need a lot more data to see it. But right now, with what we're seeing and what we've presented for vibostolimab, we're encouraged that across a potentially broad range of tumors, vibostolimab plus KEYTRUDA can add real benefit over KEYTRUDA alone.

Roy, anything you'd like to add to that?

Roy D. Baynes - Merck & Co., Inc. - Chief Medical Officer

I think that's a fulsome answer, Roger. Nothing to add.

Operator

And for your last question, it will be coming from Mara Goldstein from Mizuho Securities.

Mara Goldstein - Mizuho Securities USA LLC, Research Division - MD of Equity Research Department

Just on MK-4830, can you share with us which tumor types have responses? And just the underlying biology that might suggest this synergy between an ILT4-directed drug and the currently known checkpoint inhibition mechanism.

Roger M. Perlmutter - Merck Research Laboratories - President

Right. Thank you, Mara. The underlying biology has to do with the observation that myeloid-derived suppressor cells, cells that are of the myeloid lineage, non lymphocytic cells, in the tumor microenvironment, when abundant, can seemingly inhibit T cell responses, CD8 responses to tumors. So this is part of a fairly large program. We have a huge number of different molecules that we've been advancing preclinically. And what we found was ILT4 and some other antibodies that ILT4 is further advanced preclinically has an effect on the tumor microenvironment that seemed to relieve some of the suppression that's seen in these admittedly contrived systems.

And so the question was, could we see anything like that in a clinical setting? And the answer is yes. We're still just beginning to see. The initial studies, of course, are done in a salvage context with patients who have a lot of different tumor types, and I don't want to provide an inventory of them, but I would just say that with respect to 4830, it appears that it could be broadly active and could partner with KEYTRUDA in a number of different settings to provide improved activity.

Peter Dannenbaum - Merck & Co., Inc. - VP of IR

Great. I just want to thank you all for your interest and participation in the call today as well as your patience with respect to Q&A. If you have any follow-up questions, certainly reach out to the IR team any time. Thank you all.

Roger M. Perlmutter - Merck Research Laboratories - President

Thanks. Bye-bye.

Roy D. Baynes - Merck & Co., Inc. - Chief Medical Officer

Thank you. Bye-bye.

Operator

Thank you so much, presenters. And again, thank you, everyone, for participating. This concludes today's conference. You may now disconnect. Stay safe.

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