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EDITED TRANSCRIPT

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OVERVIEW:

Company Summary

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PRESENTATION

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Good evening, everyone. Welcome to the Investor Event of Merck and Company, Incorporated, Rahway, New Jersey, USA at the European Society of Medical Oncology Annual Meeting. Thank you to all of you who've made the effort to be with us here in Madrid and thank you to everyone tuning in via the webcast.

We're, obviously, very excited to have this opportunity to speak to you about the data that was presented this weekend in our oncology program. So during today's call, a slide presentation will accompany our speakers' prepared remarks and has been posted to the Investor Relations section of our website.

And before we get started, we'd 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 US Private Securities Litigation Reform Act of 1995. Such statements are made based on the current beliefs of our company'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. Please reference this slide in our presentation and our 2025 10-K, which identifies certain risk factors and cautionary statements. So again, thank you for coming tonight.

Dr. Eliav Barr, Senior Vice President, Head of Global Clinical Development, and Chief Medical Officer will begin our program with opening remarks. And then Dr. Marjorie Green, Senior Vice President, and Head of Oncology, Global Clinical Development will provide an overview of the key data updates we presented at ESMO. Eliav will then return with a few closing remarks before we get to all of your Q&A.

And with that, I'm happy to turn it over to Eliav.

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

All right. Well, thank you, Peter, and thanks to all of you for joining us. It's a real pleasure to be here at ESMO and to have a discussion on the ongoing progress of our oncology portfolio. This has been a really amazing, tremendous ESMO for our company. We've had three Presidential Symposium presentations that I think in many ways reflect the way in which we've been working to accomplish across the oncology portfolio.

And before Marjorie reviews the individual data sets, I'd like to take a step back and put them in context of that broader strategy. Now, as many of you know, in 2021, we outlined two strategic objectives to sustain durable leadership in oncology.

First, we sought to maximize the impact of KEYTRUDA and continue to move into earlier stages of disease where we believe we have the greatest impact on long-term patient outcomes. We also committed to diversifying our oncology pipeline with innovative investigational candidates with novel mechanisms, and these objectives continue to guide our oncology strategy today.

Now over the last several years, we've expanded KEYTRUDA's impact across tumor types and treatment settings, including through the introduction of KEYTRUDA QLEX, which may offer patients and providers a more convenient administration option compared to KEYTRUDA while providing a comparable efficacy and safety profile to KEYTRUDA.

At the same time, I think we've built a broad pipeline of innovative assets designed to address important biological drivers of cancer and potentially improve outcomes for patients across a wide range of malignancies.

So today, we believe that we are uniquely positioned to advance cancer care through a differentiated portfolio, spanning three complementary pillars of biology. The first is Immuno-oncology, where we continue to build on our leadership with KEYTRUDA while advancing next-generation approaches such as intismeran autogene and MK-2010.

The second is Precision Molecular Targeting where we're pursuing therapies directed at key oncogenic drivers and disease pathways. The third is Tissue Targeting, including antibody drug conjugates, T-cell engagers designed to deliver potent therapies precisely to tumor cells.

Importantly, these aren't isolated programs. Our strategy is to develop medicines that can stand on their own but also work together through rational combinations informed by biology and clinical experience, and increasingly sophisticated understanding of the disease. This approach allows us to build treatment paradigms that potentially improve efficacy while expanding the number of patients who might benefit from these medicines.

Now the breadth of our portfolio and the diversity of mechanisms represented within it provide us with a strong foundation for long-term innovation. Underlying all of our developmental efforts are several core principles. First, we believe that the best outcomes are often achieved when therapies with different and complementary mechanisms are combined or used sequentially.

Second, we're committed to improving therapeutic precision through biomarker driven approaches that help identify patients who can benefit the most. And then third, we continue to prioritize earlier stage and potentially curative settings where the opportunity to change the course of disease may be the greatest.

These principles have shaped our development philosophy across the portfolio, and they're reflected in the programs you'll hear today. Importantly, the data being presented at ESMO provide additional validation to this approach and demonstrate meaningful progress across several of our most important oncology programs.

So without further ado, I know you want to hear about the data sets. I'll turn it over to Marjorie.

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

Thank you, Eliav. And hello all, y'all. I hope you've been surviving ESMO and the fun of the marathon at sprint speed. As I look across our oncology portfolio today, what strikes me is how much it's evolved over the last decade. And many of our most important scientific presentations historically centered on KEYTRUDA, and rightfully so.

Throughout the KEYTRUDA program, we fundamentally changed the treatment landscape for many cancers and developed a deeper understanding of how immunotherapy can benefit patients across different tumor types.

Today, KEYTRUDA continues to be an important part of our strategy. We remain focused on extending benefit into earlier stages of disease, understanding long-term outcomes, and identifying those patients most likely to benefit from treatment. But what you're seeing at ESMO this year is also the next chapter of our oncology story.

The experience we gained through the development of KEYTRUDA has shaped how we think about biomarkers, combination approaches, earlier intervention, and precision medicine. And it's directly informed our investments in areas such as individualized neoantigen therapy and antibody drug conjugates. In many ways, the data we presented demonstrates how we are applying the lessons of the first generation of immuno-oncology to the next generation of cancer medications and combinations.

So data was highlighted by three Presidential Symposia. INTerpath-001 demonstrates the promise of individualized neoantigen therapy. Continued evolution of the treatment approach is enhancing immune targeting of cancer and represents the first Phase 3 data for INT plus KEYTRUDA in the adjuvant setting for certain patients with melanoma.

TroFuse-005 demonstrates the potential of sac-TMT in certain patients with advanced or recurrent endometrial cancer and marks the first global Phase 3 study from our broad program of 18 global Phase 3 trials.

And finally, the third presentation was KEYNOTE-C93, advancing our understanding of how to optimally use KEYTRUDA and certain types of endometrial cancer. Together, these studies reflect both the promise of our existing portfolio and the emergence of new platforms built upon lessons learned through KEYTRUDA development that have the potential to benefit patients across a broad range of cancers.

So let me start with sac-TMT, which is one of the broadest development programs currently underway in our oncology portfolio. You've heard us describe that each ADC is unique. Not all ADCs are the same. And ADCs are generally designed to deliver highly potent cytotoxic therapy preferentially to cancer cells versus normal tissue.

Differences in molecular design of an ADC can have important implications for clinical performance. What particularly excites us about sac-TMT is the thoughtful design of this molecule. Sac-TMT is a TROP2-directed ADC with a belotecan-derived topoisomerase I inhibitor payload and unique bifunctional linker that we brought in through our partnership with Kelun-Biotech.

The linker includes an irreversible connection to the antibody intended to minimize payload loss in the circulation, along with a pH-sensitive release mechanism designed to facilitate intracellular and intratumoral delivery within tumor cells and supporting bystander effect. This design is also supported by a drug to antibody ratio of approximately 7.4. So it's not just the potency of the payload that's important, it's the totality of the structure of the antibody-drug conjugate that you need to pay attention to, and we think this one is very special.

And based upon the clinical experience generated to date, the encouraging data presented by Kelun and the first global Phase 3 from our TroFuse program, we believe sac-TMT has the potential to become a cornerstone ADC across multiple tumor types. Today, we'll talk about the first global Phase 3 data from the TroFuse development program.

It's important to understand the clinical context of endometrial cancer, which remains an area of significant unmet need. It is the sixth most common cancer in women globally, and unlike many cancers, it's one of the cancers that's rising in incidence, and mortality continues to rise.

According to the American Cancer Society, there are an estimated 68,000 new cases of endometrial cancer per year, and more than 14,000 deaths from endometrial cancer in the United States are anticipated in 2026. Endometrial cancer is not only a growing significant health challenge, it's also associated with significant health care disparities. Mortality rates among black women remain approximately double of those amongst white women.

Before the introduction of immunotherapy and KEYTRUDA had its first accelerated approval in 2019, patients' outcomes who had endometrial cancer that were current were quite poor with survival ranging between 12- to 24 months. Since then, we've learned a great deal about the importance of understanding the biology of endometrial cancer, biomarkers such as mismatch repair status and KEYTRUDA-based regimens. And these have fundamentally changed outcome for many people with endometrial cancer.

The challenge is that once the endometrial cancer has progressed after chemotherapy and an anti-PD-1 or PD-L1 immunotherapy, treatment options become very limited, and survival is typically measured in months rather than in years. And that was the unmet need that TroFuse-005 was designed to address.

TroFuse-005 is our first global Phase 3 study with sac-TMT that's been presented, demonstrated a statistically significant and clinically meaningful improvement in all three clinical endpoints of progression-free survival, overall survival, and overall response rate when compared with treatment of physician's choice, which is single agent chemotherapy. And this occurred in certain patients with recurrent or advanced endometrial cancer.

It reduced the risk of disease progression or death by 41 percent and reduced the risk of death and improved overall survival and reduced that risk by 32 percent. The progression increase from 3.9- to 7.2 months is important for these people. But what I was very encouraged by was that absolute improvement of a near 7-month improvement in overall survival for people whose lifespans had been measured in usually less than a year and in months.

And so, we're getting up to 19 months in this end stage setting for many people diagnosed with endometrial cancer. The overall response rate doubled going from 17.3 percent or almost doubled to 35 percent. And another thing that I'd like to highlight is the duration of response of 11.1 months. And it's that duration of response combined with that overall response rate that really translates to that clinically compelling efficacy that was seen.

Equally important, the responses were very deep and the durability I just talked about. So I think that this data represents a meaningful advance for these people with advanced endometrial cancer who have received a platinum-based therapy and a PD or PD-L1-based treatment. And treatment options are quite limited for them. So this is exciting information for us to see and potentially gives hope to people with this disease.

The safety profile of sac-TMT is very consistent with previous studies of sac-TMT and no new safety signals were noted. Discontinuation rates were quite low. It was 3.1 percent in the sac-TMT arm and 4.9 percent in the Treatment of Physician's Choice arm and quality of life was maintained over time.

These findings represent the first and only positive global Phase 3 data for a TROP2 ADC or any ADC in endometrial cancer and reinforce our belief that sac-TMT has the potential to become an important treatment option for certain patients with advanced or recurrent disease.

Now I'm going to turn from endometrial cancer in the TroFuse-005 study to sac-TMT of lung cancer. As many of you know, our collaboration with Kelun has generated an extensive body of clinical evidence evaluating sac-TMT across multiple tumor types and treatment settings.

At ESMO, Kelun presented encouraging results from OptiTROP-Lung06 study. This was conducted in China in patients with first-line advanced non-squamous, non-small cell lung cancer whose tumors have a PD-L1 TPS below 1 percent. These are the patients who have the worst outcomes with the KEYNOTE-189 regimen and have the need for new therapies.

While pembrolizumab and chemotherapy has improved outcomes, prognosis for this population remains challenging. Median progression-free survival is approximately six months and median overall survival approximately 15 months. And what makes this study particularly interesting to me is that it evaluates sac-TMT plus pembrolizumab against a very active control arm, which is the KEYNOTE-189 control arm of pembrolizumab in chemotherapy.

And the combination demonstrated a statistically significant and clinically meaningful improvement in progression-free survival, reducing the risk of progression or death by 51 percent. Median progression-free survival improved from 5.7 months to 15 months and the duration of response was approximately doubled. Overall survival remains immature, but we observed a favorable trend with a hazard ratio of 0.58.

Safety profile also very consistent with the known safety profile of the individual agents and no new safety signals were seen. This study adds to the growing body of evidence supporting the activity of sac-TMT in non-small cell lung cancer across different PD-L1 expression levels.

Importantly, these findings, along with the other data sets evaluating sac-TMT in lung and in other tumors, provide additional confidence as we continue advancing our global TroFuse lung cancer and broader TroFuse studies.

And it supports our ambition to establish sac-TMT as a cornerstone asset and therapy across a broad range of tumors, recognizing that most oncologists in the community setting see people with multiple different kinds of cancers. Our TroFuse program currently includes 18 ongoing global Phase 3 studies and represents the broadest range of disease settings being explored for a TROP2-directed ADC.

Approximately 10 of these studies are focused on women's cancers, including endometrial, ovarian, cervical, and breast cancer. We are also pursuing opportunities across lung, bladder cancer, and gastric cancer, where TROP2 biology may provide a compelling opportunity for intervention.

Just as KEYTRUDA development taught us where immunotherapy could have its greatest impact, every sac-TMT study provides insights that shape future development decisions. These lessons are already informing for additional studies, novel combinations, biomarker strategies, and earlier stage development opportunities. And we expect the program will continue to evolve as new data emerges.

So let me then transition to the question I think you all have, let me talk about MK-2010. When I think about our overall oncology strategy, it begins with developing medicines that demonstrate meaningful activity individually and then thoughtfully combining them in ways that may improve outcomes for patients.

We believe that Merck is uniquely positioned to evaluate this biology given our extensive experience with KEYTRUDA, our history of developing VEGF-containing regimens, and the breadth of assets available for the combination development within our portfolio. Today, multiple Phase 2 combination studies are underway about MK-2010 alongside assets such as sac-TMT, WELIREG, and other therapies.

As we have said in the past, MK-2010 is a Phase 3 ready asset. We have had productive discussions with the FDA regarding our Phase 3 plans. Based on those discussions and the totality of data generated to date, we anticipate initiating Phase 3 development for MK-2010, including combinations with sac-TMT in the first line non-small cell lung cancer setting in the first half of 2027. We will provide further updates on these plans in due course.

Turning now to intismeran, our individualized neoantigen therapy with our partners Moderna, which I believe this is one of the most exciting scientific advances in oncology today. One of the most important lessons we learned is that durable clinical benefit depends upon effective immune recognition of tumor-specific antigens. So we've learned a great deal about what the T-cells need, and we use PD-L1 and scores like GEP to understand that, and we understand the importance of the tumor mutational burden in development of tumor-specific antigens.

And intismeran was purposely designed around the principle that using a patient's own tumor sample, we can identify the unique mutational fingerprint of their cancer and generate a personalized mRNA-based therapy encoding up to 34 neoantigens specific to that individual patient.

The goal is to create and expand tumor-specific T-cell responses and complement the immune activation that already is generated by KEYTRUDA. This represents a fundamentally individualized approach to cancer therapy. Rather than targeting a single shared antigen, each therapy is designed to be tailored to the specific biology of an individual patient's tumor.

And at ESMO on Saturday, we presented results from INTERpath-001, which represents an important milestone both for us and excitement for what a research program can mean for the broader oncology field. This is the first positive Phase 3 study of an individualized neoantigen therapy and the first positive Phase 3 study of an mRNA-based cancer therapy for certain patients with melanoma.

Patients with high-risk resected melanoma remain at risk for recurrence despite significant advances made with checkpoint inhibitors. Before immunotherapy, thinking back sort of 2010 and even earlier, three-year recurrence rates exceeded 65 percent for many people with high-risk melanoma. KEYTRUDA and other checkpoint inhibitors have improved outcomes for people with resectable high-risk Stage 2 through 4 melanoma, yet unmet need remains.

In INTERpath-001, intismeran plus KEYTRUDA significantly reduced the risk of recurrence or death by 42 percent and reduced the risk of distant metastasis or death by 38 percent compared with KEYTRUDA alone. Improvements were observed across recurrence-free survival and distant metastasis-free survival, and results were generally consistent across subgroups.

The safety profile also was very consistent with what was seen in KEYNOTE-942 and no new safety signals were identified. What we are seeing in Phase 3 builds upon the body of evidence previously generated in KEYNOTE-942, our Phase 2B study evaluating intismeran in combination with KEYTRUDA compared to KEYTRUDA alone for patients with Stage 3B, C, and 4 resected melanoma.

The sensitivity analysis that were done help us understand the shape of recurrence-free survival and distant metastasis-free survival curves. There are two distinct periods, and you think about when checkpoint inhibitors first emerged that people had to be taught about non-proportional hazards in the oncology space. And I think that paying attention to this is important because we are doing something that's novel in the oncology area but is seen in other therapeutic areas.

During the first six months, the curves are largely overlapping with hazard ratios of 0.99 for RFS and 1.01 for DMFS. After six months, the curves separate with hazard ratios improving to 0.42 for RFS and 0.50 for DMFS. This pattern is biologically consistent with what we understand about therapeutic vaccines.

Unlike a directly cytotoxic therapy, an individualized neoantigen therapy requires time to prime and boost and repeatedly boost the immune response, expand neoantigen-specific T-cells, and overcome the anergic or suppressed state created by the tumor microenvironment.

In the Phase 2 KEYNOTE-942 study, data presented an exploratory analysis of a random subset of patients at AACR in 2025 and then at ASCO in 2026 show a rise in T-cells in the first five- to six months after starting intismeran through those repeated doses when compared to the pembrolizumab control arm.

The two components of the regimen are intended to play complementary roles. And intismeran is designed to generate and expand the T-cells directed against neoantigens unique to an individual patient's tumor. Pembrolizumab removes the PD-1 mediated inhibition, enabling those T-cells to remain active against the cancer. The early overlap in the curves, therefore, is not unexpected. During that period, the immune system is being -- memory response is being primed and boosted.

Once a sufficient immune response is developed, the event pattern changes meaningfully with hazard ratios in the 0.4 to 0.5 range beyond six months. We have seen the importance of priming and boosting with preventative vaccines, including GARDASIL. While this is a therapeutic cancer setting and the biology is more complex, the underlying principle is similar. Repeated exposure may be needed to generate a sufficiently robust immune response, particularly when trying to overcome pre-existing immune suppression.

This is a pre-specified sensitivity analysis and does not replace the ITT analysis, which is so important in oncology studies. However, it strengthens our confidence that combination is generating a meaningful immune-mediated treatment effect.

INTerpath-001 is only the beginning. One of the things we've been very deliberate about with INT is how we built the development program. We focus first on tumor types where immunotherapy is already established, and that slide needs to probably progress because you can't see the whole program here, let me try and see.

We focus first on tumor types that immunotherapy is already established, and we believe an earlier intervention provides the greatest opportunity because I lost my place. We now have multiple late-stage studies underway across melanoma, lung cancer, bladder cancer, and renal cell carcinoma with multiple studies already enrolled.

These trials would be important for signal detection to help us understand the role of INT across tumor types of different biological characteristics, including tumor mutational burden and varying sensitivity to immunotherapy across disease types, and also in settings as we have studies in the metastatic setting ongoing as well.

We are also looking at INT as monotherapy and in combination with other drugs such as TICE BCG. As examples, melanoma is a tumor that has high tumor mutational burden and is highly sensitive to IO therapy, whereas renal cell carcinoma, which is IO-sensitive, has lower TMB and potentially lower neoantigen expression. The positive Phase 3 results we have seen in melanoma represent a proof point for the platform.

As additional studies mature, we look forward to sharing more data and further defining the potential of individualized neoantigen therapy across oncology. As we think about the future of oncology, we increasingly see opportunities to combine complementary mechanisms and rational ways that may further improve outcomes for patients.

So when you step back and look across our data presentations at ESMO this year, you begin to see the future taking shape. Together, these programs represent the next chapter of our oncology program and our continued commitment to bringing innovative therapies to patients with cancer.

And with that, I'll turn it back to Eliav.

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

All right. Well, thanks, Marjorie. So as you've heard today, the data presented at -- yeah, I know. I mean, seriously. If we fall, can someone just make sure that we don't get a neck brace? Anyway, so anyway, back to business.

As you've heard today, the data presented at ESMO reflect meaningful progress on several of the programs we believe will help define the next chapter in our oncology portfolio. Whether it's sac-TMT, intismeran, MK-2010 or the broader portfolio, we really remain focused on advancing therapies that have the potential to address important unmet needs and improve outcomes for patients living with certain types of cancers.

The data we've seen today are not isolated achievements. They're the results of a deliberate strategy we established several years ago, maximizing the impact of KEYTRUDA, extending our leadership into earlier stage of disease, building a diversified oncology portfolio spanning multiple biologic pathways, modalities, and mechanisms of action.

The progress highlighted today reinforce our confidence of this strategy and also the ability to continue to deliver meaningful innovations to patients. Looking ahead, we see the potential of two important oncology approvals next year. First, sac-TMT. As you heard, has now generated positive Phase 3 data in certain types of endometrial cancer through TroFuse-005.

It's exciting that this is the first global Phase 3 study within the TroFuse development program, an important milestone in what we believe could become a cornerstone ADC across multiple tumor types. The FDA has granted a PDUFA date of June 15, and of course, we look forward to continuing to work with regulatory authorities to bring sac-TMT to patients as quickly as possible.

Second, intismeran autogene has delivered the first positive Phase 3 for an mRNA-based individual neoantigen therapy in melanoma. And that's really strengthened our belief in the potential of this approach and further supports ongoing expansion of the INTERpath program. We're waiting for these efficacy results to really send things into a bigger trajectory. Based on these data, we're already engaging with regulatory authorities, and we look forward to hearing their thoughts.

Now beyond these near-term opportunities, what really excites us most is the breadth and depth of the oncology pipeline that continues to advance behind these lead assets. We see a substantial and diversified set of registration-enabling opportunities extending through the remainder of the decade. Those opportunities span all three strategic pillars, the Immuno-oncology pillar, the Tissue Targeting pillar, and the Precision Molecular Targeting pillar.

They include multiple potential first or best-in-class approaches and encompass a broad range of modalities, including ADCs, antibody-drug conjugates, individual neoantigen therapies, T-cell engagers, targeted small molecules, and then next-generation immunotherapies.

What's particularly important is that many of these programs are being developed not only as standalone, but also as rational combinations, informed by the more than decade of experience that we've had with KEYTRUDA and a growing understanding of tumor biology. That approach continues to guide how we think about maximizing benefit for patients and creating the next generation of oncology treatment paradigms.

Taken together, we believe the data presented at ESMO and the development opportunities ahead reinforce our confidence in our oncology strategy and our ability to continue to deliver meaningful innovation for patients over many years to come.

With that, I'll turn it over to Peter for Q&A and we'll gingerly walk back to my chair.

QUESTIONS AND ANSWERS

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

Okay. Questions? Hayley and Aye from my team have microphones. So if you please wait for a mic and when the mic comes to you, if you could state your name and firm, that would be really helpful to all of us here and online. So Akash.

Akash Tewari - Jefferies LLC - Analyst

Thanks so much. Just one quick one and a more in-depth one. The PD-1 VEGF combo with sac-TMT. Does that mean we're not necessarily going to get sac-TMT pembro first line lung studies? I just want to make sure we clarify that.

And then for maybe the cancer vaccine, are we going to look back maybe 5-, 10 years from now and think the analogy was not about this being a metastatic or even a post-resection drug, but maybe something more similar to GARDASIL?

Like you're running a study in a high-risk Stage 1 setting. You're talking about running monotherapy trials as well. We have seen monotherapy kind of durable neoantigen responses. So are we too focused on renal and we really should be looking about going in a pre-cancerous, maybe polyp-like setting with this drug?

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

So maybe I'll ask Marjorie to take the first one, and I'll take the second, the vaccine. Yeah.

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

Yeah, I think that the data that we've seen from our partners, Kelun, with sac-TMT, and pembro is quite compelling. And so I see why you're answering the question. And part of it, we haven't disclosed the design of what the study would look like. Because you think about contribution components, you think about potential like really wonderful kind of combinations out there.

We do think that the data that's been generated to date with VEGF bispecifics in regards to PFS has been really clinically meaningful and compelling and improved therapeutic index. And so if your goal is really to displace KEYNOTE-189, you want to make sure you're optimizing your chances. And so I say stay tuned to what the study design is going to be.

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

And on the broader question, I think you are right that the nature of INT really remains to be defined. The way our development program has been set up is to try to address a lot of those questions. And in fact, there is a study now that is looking at earliest stage cancers. Now of course these studies take quite some time to read out but I think we invested right at the beginning or at the outset of that.

I am eager to look at opportunities for INT outside of KEYTRUDA simply because KEYTRUDA, while being wonderful, still has an AE profile that requires careful attention. And so, we've already started to look at that in non-muscle invasive bladder cancer, a combination with BCG. But I think that there's going to be opportunities, as you note, earlier on.

I think the most important thing we need to address, and there's a lot of work that's being done right now, is to understand how the algorithm worked. The algorithm worked really well, there's no doubt about it. But the amount of data that we're going to be able to crunch now will really tell us a lot about what we need, what are the optimal directions that we're going to go. And I expect, I anticipate that 2027 will have some really interesting studies.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

Great. And for the record, that was Akash Tewari from Jefferies. It's okay. Asad.

Asad Haider - The Goldman Sachs Group, Inc. - Analyst

Great. Asad Haider, Goldman Sachs. Thanks for taking the question. Just going back to INT on overall survival for the OptiTROP-Lung06, that demonstrated a notable trend, hazard ratio of 0.77, albeit it was still fairly immature. So do you see the potential for OS to meet stat sig given powering? The discussant said that no other adjuvant trials have shown this in melanoma have shown in OS benefits so far.

And then just is the level of benefit shown compelling for payers in the context of, just competitive neoadjuvant regimens? Just any high-level thought there?

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

I think they're related topics. So if you look at the checkpoint inhibitor study, so looking at, for example, KEYNOTE-054 and looking at the adjuvant pembrolizumab studies, significant clinical benefit has been seen that they have not yet improved overall survival. And even though melanoma is a disease that can affect the young, about a third of patients diagnosed with melanoma are quite young at diagnosis, the median age is still around 60 or 61.

And this is part of why we showed the distant metastasis-free survival, because that effectively indicates people who do have disease that is likely going to be fatal or has the potential to be fatal. And when that happens, there's significant burden, not only for the trauma to that

individual, but thinking about it from a health care system, that someone has to have biopsies and PET scans and CAT scans and additional therapies and loss of productivity. And just everything horrible that happens with recurrent cancer, and that's a very strong surrogate.

In the curative setting, our goal is to get people's survival to where it matches age-related survival. Unfortunately, our cancer therapies can't keep things like heart disease and Alzheimer's and motor vehicle accidents from happening. And so, I hope that we will see overall survival, and us seeing DMFS at the first interim analysis is quite interesting and compelling, but it's going to take time to know whether we are going to see that for certain.

I think that then relates to your question about payers. I think that there is a significant burden by having recurrent disease and that distant metastasis-free survival, I think, is the compelling reason when you think about what would happen if somebody did develop liver metastasis or lung metastasis and the downstream consequences of that. Anything else you'd like to add, Eliav?

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

Yeah, I think, the 0.77 number was -- really is exciting. It's small numbers and so we really have to have those data mature. As somebody who's been sitting around waiting for KEYNOTE-054 to read out, the problem now is for the past four years, all the deaths have been heart disease and that kind of stuff. So no secondary malignancies.

But it's all been sort of deaths. And death is death, but it's not cancer deaths. So we're going to look at cancer-free survival as a kind of a surrogate, but I think the DMFS is probably the best way to look at that. And so, time will tell, but it's very encouraging.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

Terence.

Terence Flynn - Morgan Stanley & Co Ltd - Analyst

Thanks so much. Terence Flynn, Morgan Stanley. I guess a two-part for me. I was just wondering, Eliav, if you can comment on, from the melanoma data, what gives you confidence in RCC, MIBC? Those are the next two readouts that we're going to see here. And then maybe I thought the PDAC poster was pretty interesting, particularly given low TMB. So what are the implications of that for the next set of tumors? And then can RCC and MIBC be registration-enabling? Could you file on those potentially? Thank you.

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

Sure. Maybe we'll talk about the broader points and then talk about the specifics. I mean, look, we're in a new era. This is really groundbreaking therapy. And so, when we designed the clinical program, we tried to address archetype diseases that would enable us to get a certain feel about the breadth of this, almost like trying to feel our way to work at the outer limits of what INT could do.

We reasoned from the beginning that the most important thing was to have a relatively intact immune system and to try to do this in a curative setting where the patients haven't yet received strong anti-cancer therapies which in and of themselves can cause long-term harm. And so with that in mind, we then looked at the KEYTRUDA data and the KEYTRUDA data had some surprises and the surprises in KEYTRUDA was that you didn't need to have high tumor mutational burden kind of cancers to have KEYTRUDA efficacy, and in fact RCC is that archetype.

And so you can take the tumors that are high or relatively high TMB and you look at non-small cell lung cancer and melanoma and they've got pretty high, they're all smoking related stuff, so it's very pretty high TMB. And MIBC is not terribly different than that. I mean, it's a little bit less TMB, but it's also very much a carcinogen-driven disease with high responsiveness to pembrolizumab.

RCC, I think, was a deliberate step to ask the question about -- can you be INT-responsive and not be high TMB? We've been actually pretty successful in getting good neoantigens in that trial. Whether we're going to be, whether that's going to translate to efficacy, one doesn't know. And that's why we did it as Phase 2 trials as opposed to Phase 3, which then speaks to your second question.

Which is, as the MAH, the party of record in front of the agencies, Phase 2 trials are Phase 2 trials. And, we don't want to get ahead of the regulatory authorities and presume anything. The data, such as they are, will be -- I think will be -- I hope will be compelling, and then we'll see.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

Daina.

Daina Graybosch - Leerink Partners LLC - Analyst

You have to get your melanoma patients on enlicitide, so you --

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

No kidding.

Daina Graybosch - Leerink Partners LLC - Analyst

Daina Graybosch from Leerink Partners. One quick technical question, and then a less technical one. So the non-proportional hazards, you saw that also in KEYNOTE-942, the Phase 2. And I wonder if you've talked to regulators about using statistical models as your primary analysis that reflect that. So something that's not a proportional hazard model.

And then the less technical question. On TroFuse-005, very interesting in the subgroup that you saw an association of TROP2 expression with the TROP2 medium and high seeming to derive more benefit. I wonder if you could talk to that and if you have any plan for using that biomarker in your gynecological development of the ADC?

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

So maybe starting first with the question about INT and the non-proportional hazard. So I do think, again, the FDA is very familiar with these kinds of curves. And so we have not talked about our discussions with the FDA, and I don't want to get ahead of what may end up in a potential label or how this would show up in there. But we wanted to really help to start to educate the broader community in oncology about this.

Thinking back as an oncologist, I know in theory how vaccines work, and this is a therapeutic, and so you're combining these two kinds of pieces together, and it's helping to introduce this to people. So as we generate more data, and we sell the great durability in KEYNOTE-942 of that very durable, sustained response over five years, we're imagining what's going to happen at seven years and longer, and the same thing with INTerpath-001.

So I think it's stay tuned would be my answer, Daina, on that as we talk to health authorities, but this is something the FDA and other health authorities, I think, are going to be familiar with.

In terms of the biomarker subgroup and TroFuse-005, and the discussant today got privy to some of the data that was there. And endometrial cancer is a tumor type that has very high expression of TROP2. Responses were seen across all expression level of TROP2, even people

who had minimal or no detection. And that's because you do get inherent bystander effect with TROP2 -- in this TROP2 ADC. And so you do get activity there.

And the way that the histology worked out is that carcinosarcoma tumors tend to have lower TROP2 expression than those tumors that are not carcinosarcoma, and those tumors are biologically quite aggressive. The response rate was higher in carcinosarcoma with sac-TMT than it was with the control arm, but that does impact those results between the higher TROP2 expression and the lower TROP2 expression on those hazard ratios.

In both groups, though, clinically meaningful results we're seeing compared to control across all levels of TROP2. And so I think this is a drug that has benefit across all the subgroups that were studied in the trial.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

Great. Chris.

Christopher Schott - JPMorgan Chase & Co. - Analyst

Great. Thanks. Chris Schott, JPMorgan. Just on sac-TMT, just a question on the drug. Maybe broadly in first-line lung given the ASCO data and now the ESMO data, maybe specifically how you're thinking about the PD-L1 kind of lows, the 1 through 49s. Should we think about Merck developing kind of broadly or would you want to explore that as milli group to see what the proper kind of approach would be in that setting?

And maybe just a quick second one, which is the translation of some of the China data we've seen on sac-TMT to global studies. I think we saw the first one of these today, but just like a little bit about on endometrial, how that played out versus what you had seen from China and just what confidence that gives you for the broader global studies?

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

Thank you. When you look at the registration studies that are ongoing right now with sac-TMT, remember we started these studies about three-ish plus years ago. And we had initial data, another Phase 3 data that we're seeing from Kelun was available at the time. We had a lot of Phase 2 data that we were co-generating together and some initial data from Kelun.

And so we went into some settings where we really thought as a maintenance approach that we would be able to have tremendous benefit. And that includes those people who have higher PD-L1 expression in their tumors as well as those who don't necessarily. And so we do have maintenance approaches for across all of the ranges in KEYNOTE-189.

I think the question you're getting to is if we were going to do a replacement strategy, would we focus on a higher tumor, PD-L1 tumor population or an all-comer? And I don't want to talk about potential future phase 3s too much until they hit clinicaltrials.gov, but there's unmet need across all expression levels. There's a question about where would you get your biggest bang for your buck with a therapy. And I think that when you look at all of the data sets that Kelun have generated, there has been consistent, compelling efficacy in every subgroup that has been evaluated by sac-TMT. And so, it's really exciting.

And that goes into your question of, well, how much can you trust the data and how it translates into global studies? There is data presented at ICGS this year of the TroFuse -- it wasn't TroFuse, it was 2870-001 was the name of the study. It was a very, very large Phase 2 study that we were working with Kelun together to help explore all of these tumors that have been formed for 18 Phase 3 studies.

And the data from the endometrial cohorts was presented and it looked at four milligrams per kilogram and five milligrams per kilogram because we wanted to understand fully where was the best benefit risk for something that we thought had the potential to go broadly and understand the efficacy.

And the data presented there, it was a slightly different patient population than in the Phase 3 study, but you see very generally consistent response rates and duration of response. And antibody-drug conjugates tend to be quite consistent when in similar-ish populations of response rate and duration of response. And those are the things that translate into meaningful long-term outcomes.

Same thing is true about the safety. And so when you look across different studies, so example, the breast study that was updated the Phase 3, you look at the stomatitis rate that's in that study is very similar in that trial to what we see in TroFuse-005. Whereas in the Phase 2, the stomatitis rate was a little bit lower. So we're seeing consistent data in the disease studied in the Phase 2 China study that has translated into global Phase 3 endometrial study.

The thing about global studies is that you do have heterogeneity of populations. You have heterogeneity of AE management. You have subsequent therapies that are different across the globe. And so each trial will be its own experiment. But I think that consistency and seeing that positive data and what really makes me excited is that durability of being able to deliver it for a long time makes me very optimistic about the program broadly.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

Great. Carter.

Carter Gould - Cantor Fitzgerald LP - Analyst

Carter Gould with Cantor. First, a clarifying question, and this may be -- I just want to make sure I'm capturing this correctly. It looked like your HR-positive breast strategy may have been updated. I believe TroFuse-010 was supposed to be a frontline and second-line study, and slides are at least showing that only is frontline now. I just want to make sure that's correct.

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

It's frontline. It's a frontline study, yes. I think that -- it's a frontline study.

Carter Gould - Cantor Fitzgerald LP - Analyst

Still same size and still data next year?

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

We have not. I'd say go to ct.gov for the clarity.

Carter Gould - Cantor Fitzgerald LP - Analyst

All right. Perhaps more importantly, there was a lot of conversation with the discussant, whatever day that was, a day or two ago on the INT regarding neoadjuvant use of PD-1s. I want to give you a chance to comment. I know I've talked to Eliav and Dean about that before, but it was a couple of years ago and just now how you think about NADINA and SWOG potentially being a complicating factor commercially.

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

The neoadjuvant studies were initially designed -- the patients with the tumors, they tended to have macroscopic sort of bigger melanomas that had lymph node involvement. Both SWOG 1801 and the NADINA study did have these larger tumors and so they -- the SWOG study also included potentially resectable Stage 4 disease. And so they are a selected subgroup of melanoma.

And part of what -- it's very hard with these Mohs microsurgery and the lymph node surgeries sometimes to get good negative margins. And so one of the questions was, could you do this and make the surgery easier and then be able to have your benefit? And then they were looking at efficacy as well. The studies you're looking, it's little apples and oranges between these trials a bit.

And so I say that, when you're looking at the NADINA study, these were well-conducted studies, both of them. In the experimental arm where people received two cycles of Ipi-Nivo, there was a -- 6 percent to 7 percent of people didn't make it to surgery. And then in the adjuvant setting, you had about 10 percent of people received monotherapy Nevo, you had people receiving BRAF-directed therapy, and you had a lot of heterogeneity in your post-adjuvant treatment. And it makes it really hard for us to look at that trial and compare what does that mean versus what does INTERpath-001 mean.

People really anchor on the 83 percent data and that was data with a median follow-up of about nine point something months compared to the two-year data that has also been published on the NADINA study that showed that that benefit, the original hazard ratio in the 0.3 something range had dropped into the 0.4 something range and then maybe it's stabilizing. It's hard to tell, but there was some lost efficacy.

So I think it's an important study and it's something that's really helped to show that for people who do have these bulky kind of diseases that you're able to do this approach, but there is risk of progression. We saw in the SWOG 1801 study, about 10 percent of people didn't make it to surgery because of progression in that period as well.

That study had more consistent adjuvant therapy and we do see a drop in efficacy over time in the adjuvant setting when you look at the first two-year event-free survival and then going into later data sets. So I can't compare them, not because I don't want to, but they are very apples and oranges in their approach.

What I can do is look at the KEYNOTE-942 study, which did have a higher risk population that we see in the INTERpath-001 study. And I see very consistent two-year data. And then in KEYNOTE-942, it's staying stable over time. And so we'll need time to see what this happens over time here or are we going to see those continued durable benefits?

The number of people who have neoadjuvant therapy, we think it's about 20 percent of the population who are really candidates for the neoadjuvant approach, and there's a lot of heterogeneity about where it's used. And so we also need to remember that for the NADINA study, about 30 percent of people get very significant grade three or higher toxicities. And there were people who were unable to either undergo surgery or receive any adjuvant therapy when they needed it because of potentially residual disease due to significant toxicity.

Whereas when we look at the toxicity with INTERpath-001, there are no increase in immune-related AEs and the therapy was generally deliverable and well tolerated.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

Alex.

Alexandria Hammond - Wolfe Research LLC - Equity Analyst

Alex Hammond, Wolfe Research. So the discussion for the OptiTROP trials mentioned dose attenuation and pulsing dosing will be part of ADCs in non-small cell lung cancer. So I guess I'm wondering if and how you guys are planning to implement those strategies into your development with sac-TMT?

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

I am sorry. Could you rephrase the question for me?

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

I couldn't hear you.

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

I have a hard time hearing you.

Alexandria Hammond - Wolfe Research LLC - Equity Analyst

If you're going to utilize dose pulsing with sac-TMT in small cell lung cancer.

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

Dose pulsing in non-small cell lung cancer. I'm not certain what they mean. I missed that presentation. I hate to tell my partners, Kelun, that I missed that presentation. So I'm going to need to listen to the discussion to understand what they intended by that.

Though there is dose modification that occurs because this is a cytotoxic therapy. And depending upon the AE profile, sometimes you can hold a dose or you can modify the dosing if needed. There isn't a current prospective plan to look at some kind of induction and maintenance. We think that we have with our four milligram per kilogram dose that we are using in our global studies, either as monotherapy in combination, the optimal kind of dosing for benefit and risk. And that's spoken to by the duration of response.

If you look at the endometrial study, the OptiTROP -- excuse me, the TroFuse-005 study, the duration of therapy there is over 30 weeks for the experimental arm compared to 15 weeks for the control arm. And despite that doubling of therapy exposure, the number of people who had to discontinue drug due to toxicity was numerically higher in the control arm.

So I think that having to modify doses is not unexpected with a cytotoxic therapy. I think that it's more important to think about, can people stay on treatment in a very tolerable way? And that duration of response shows it, and the quality of life being maintained is another thing that really is very reassuring.

You never want treatment to be worse than disease, and people who've got recurrent cancer, they're not going to take therapy that's making them miserable. And so even though they do have this very high unmet need. And so I've been very reassured and you're seeing that consistency across multiple studies in the Kelun studies as well as now in the global trial as well. I may not specifically answer your question, but that's how I think about the dosing of sac-TMT in our global trials.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

Courtney.

Courtney Breen - Sanford C Bernstein & Co LLC - Equity Analyst

Hi, there. Courtney Breen from Bernstein. Two questions, the first one's hopefully a quick answer. The sac-TMT PDUFA date that you mentioned is June 15. Can you just clarify if you're using the CNPV for that date or could the CNPV pull that further forward? It doesn't seem kind of fast enough based on the kind of previously historical, I guess, proposed timelines that might be possible with CNPV.

And then the other question that I had was just about the combination potential Phase 3s that could start in the first half of next year. You've obviously got Phase 2s ongoing. They appeared on clinicaltrials.gov last month. I think it was, but perhaps popped up a little bit earlier as well.

Can you just tell us about the burden of data that you will have to inform that decision? Or are you relying on data from Kelun, combinations with other PD-1 VEGFs and sac-TMT, internal modeling? How are you getting conviction about the dosing and the combination selections you're making?

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

So I think, as stated about, I'll address the second part first, is that we've had very productive conversations with the FDA, which is why we're just telling you that we're starting our Phase 3s next year. And so really excited about that.

Phase 2 studies are done for multiple reasons. Some of them can be signal-finding, but they also can be used to get greater understanding of combinations and inform for ongoing Phase 3 trials. And we have multiple combinations that we're looking at with 2010, not necessarily just with sac-TMT in these studies.

And so I don't want to say anything more specific than that because of the hyper-competitive landscape that we're in, but there are a lot of reasons for us to have Phase 2 studies ongoing while concurrently thinking about a Phase 3 development program or Phase 3-ready asset 2010. So lots of excitement there.

Kelun does have its own bispecific that it's working with. We have data that they've done with Avastin combined with a checkpoint inhibitor and sac-TMT. So we do have data sets that already have helped to inform for information that we're using for our global studies. And so lots of stuff that's ongoing to inform for potential future for that combination.

We've had really productive conversations here with the FDA. I never want to get ahead of them. When you submit something, whether you're using the NPV or not, you get the PDUFA date. I think that we are all very excited about the potential to accelerate. Anything else you'd like to add on?

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

Yeah, I mean, I would say that our discussions with FDA today have been incredibly productive and speedy. And we've had good experience with their very robust, very in-depth, but more accelerated reviews. So we're hopeful that we can bring this drug for patients as quickly as possible.

I also want to point out for 2010 that it's not just sac-TMT and 2010. 2010 will friends with benefits with different parts of our pipeline. So we look forward to being able to get started with that next year as well.

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

And that's part of why we have several studies is because they're different INDs.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

Dina.

Unidentified Participant

Hi, thanks. This is Dina from UBS on for Mike Yee. I guess. On the -- to Daina's point on the biomarker strategy, in the Opti-Lung06, we actually saw, while it's very stunning and great data, we did see that there was a better benefit in the TROP2 low patients, which was kind of opposite of what we saw in the endometrial. So there is a bit of a difference in the TROP2 expression and the benefit that we see across cancer types.

I guess maybe just thinking about what is your strategy for the biomarker testing. I saw on one of your slides that in lung, that you're not focused so much on the biomarker strategy, but you are in other indications. So just want to talk through how you're thinking about that.

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

Maybe to clarify, we have a broad biomarker plan across all of our sac-TMT studies. Every tumor is going to be different about expression and response. And during the presentation today with the TroFuse-005, it referenced the testing that's being done with RTD and IHC testing.

And we have very similar kinds of approaches in our studies. And we have not talked about where we might have a primary hypothesis about a biomarker enrichment or not in particular studies. And part of it has to do with how antibody-drug conjugates, particularly this one that does have very robust bystander effect as well. And different tumor types may need to have more consideration than others. And so it's there.

It's also meant to be scalable for global usage. And so that's why it's there and we're thoughtful about it, but that's all I can really tell you at this time.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

All right, so it's been a long four days. We're just over the hour mark, so maybe time for two more questions. Will.

William Zhang - Wells Fargo - Analyst

Hi, Will Zhang here from Mohit Bansal, Wells Fargo. I know you alluded to going against KEYNOTE-189 with a potential sac-TMT and MK-2010 combo. I guess like based on the data we've seen from the PD1-VEGF class and then also the old PD-1 plus VEGF combo trials, do you see like a specific histology that such a combo would make more sense and also, I guess like in squam, do you see a rationale for MK-2010 plus sac-TMT as well?

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

No. It was a very leading question, saying that we're going to go against 189 broadly. So we're doing a study in first line. And just stay tuned to next year. So I can't speak more specifically.

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

I think we're very confident. I have to say that the Kelun data --

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

Works across all histologies.

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

I mean, seriously, they're just really -- it's pretty important for us. I mean, Kelun is a wonderful -- gives us a harbinger of what to look for and what to do and not do. What's been super cool about the OptiTROP-Lung program is that, it's active here, it's active there, it's active everywhere. So I think that it provides Marjorie and her team with a lot of optionality to do smart trial design. I'm grading them and we'll see what happens next year.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

All right, last question. Richard.

Richard Wagner - Bank of America - Analyst

Thank you for the question. Richard Wagner, Bank of America for Jason Gerberry.

I wanted to return to the neoadjuvant question setting for intismeran. What is the state of the technology now with regard to the ability to turn around doses quickly in order to understand what is the practical -- what are the practical considerations with intercepting a patient undergoing neoadjuvant treatment?

I know that you are putting forward some fairly ambitious studies where you intercept patients after three cycles of preoperative chemotherapy and bladder cancer. Would that technology state now, does that open a neoadjuvant melanoma study? Would you do it if you can?

And then indirectly but still within the neoadjuvant versus adjuvant paradigm, the result, the failure to show overall survival with KEYTRUDA in the adjuvant lung cancer setting, the PEARLS study, KEYNOTE-091. What does that mean for intismeran study with KEYTRUDA in the adjuvant setting? Is adjuvant KEYTRUDA essentially a practice that will go away by the time the results are available?

Marjorie Green - Merck & Co Inc - Senior Vice President, Head of Oncology Global Clinical Development

There are lots of different questions in those two points. And so maybe let me start with talking about survival in lung cancer. And I think the presentation that was done this afternoon about the updated data from KEYNOTE-091. They talked about the lung cancer-specific survival in the same way that we were talking about the distant metastasis-free survival, and that when you have an older population, that you have competing causes of death. And they highlighted some of the death imbalances that occurred in KEYNOTE-091.

And so we do think that our goal always with therapy in the curative intent setting is to reduce the risk of death from cancer being what takes someone away prematurely compared to what would normally happen to them if all things were created equal. And so I wish that these therapies would cure heart disease and cure strokes and other things that happen, but they're not able to do that.

And so it's really important to think about the totality of burden of cancer and recurrence and outcomes when thinking about benefits of therapy, and that's how I generally view that. Our Phase 3 studies can't answer every clinical question that's out there. Just the registration studies, the way that we do them is, I can't answer them all at one time.

And so this is an open question about could you do -- would there be something for someone who has residual disease after a neoadjuvant approach? It's not used as much in the community setting. It tends to be done much more in the academic setting. And because of the need, you have to really carefully map the tumor and the lymph nodes.

And I think that there are some questions that we just don't have answers to today. And again, the majority of people do not receive neoadjuvant therapy for melanoma at this time. The turnaround time for generation of INT, it's a complex but well-oiled machine, and Moderna has been amazing partners to work with on the manufacturing and getting things up to scale. And we've had to do this in multiple global studies to get this going in a very consistent way.

So we're ready for commercialization and there's a huge orchestration process that has been done that is complex but is very scalable to get this out there. And right now we're saying the turnaround time is around six weeks. So if you have a neoadjuvant regimen that is a six week regimen. Yeah, right now those two things are not necessarily compatible. So there are things you could consider for a study concept that could introduce a neoadjuvant approach.

But I think that the data is quite consistent in INTERpath-001 across multiple stages, across multiple subgroups. And again, if I go back to the SWOG study and 10 percent of people had progression before they got to surgery in the neoadjuvant setting. I think that the data you have is quite compelling in INTERpath-001.

Eliav Barr - Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer

Yeah, I don't see neoadjuvant becoming the rage. That's not what we're hearing from our melanoma experts. It's a very specific set of patients where they really want to be able to debulk the tumor before they do the surgery. So I think that the 1801 regimen is good, is relevant for specific narrow group of patients. And I think adjuvant is going to be the way to go for most of the patients.

Peter Dannenbaum - Merck & Co Inc - Senior Vice President, Investor Relations

Okay. Thank you all again for your time and attention and the really good questions. And safe travels home.

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