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EDITED TRANSCRIPT

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OVERVIEW:

Company Summary

LSEG DATA & ANALYTICS

CORPORATE PARTICIPANTS

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CONFERENCE CALL PARTICIPANTS

Akash Tewari *Jefferies LLC - Analyst*

PRESENTATION

Akash Tewari - *Jefferies LLC - Analyst*

Good morning, everyone. Still morning? Yes, it is still in the morning.

My name's Akash Tewari. I head our pharma and biotech efforts here on the research side for Jefferies.

Joining us is Merck, a company that really global company with focus on multiple disease areas, but we have Marjorie who heads their Oncology efforts and Merck is certainly a leader there and we're fresh from coming from ASCO. So I'm really excited for this conversation.

Marjorie, maybe I'll hand it off to you for some opening remarks and we'll get to going.

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

Yeah, no, great. Thanks so much. I -- ASCO was an exciting time for Merck and for us. Our partners, Kelun-Biotech presented data from OptiTROP-Lung05, which is a Phase 3 global study looking in non-small cell lung cancer at the combination of sac-TMT combined with KEYTRUDA versus KEYTRUDA alone showing clinically meaningful improvements in progression-free survival and a trend noting immature data in overall survival for those people who have non-small cell lung cancer or with a TPS of greater than 1%.

We also had updated data sets from KEYNOTE-942, which is a combination of pembrolizumab and INT, and individualized neoantigen therapy, as treatment of people with certain melanoma, Stage II and III. And that five-year durability data was quite compelling.

We also had compelling data from the five-year update from KEYNOTE-522, looking at people who have triple receptor negative breast cancer, as well as other updates across the Oncology portfolio. So it was a great meeting for Merck, and there's a lot of really exciting external data as well, which made it a fun time and helps us to be excited about our continued path forward.

QUESTIONS AND ANSWERS

Akash Tewari - *Jefferies LLC - Analyst*

Understood, and I certainly agree. It was definitely a good ASCO for Merck.

I wanted to start on lung, and I'll take it from a different angle, which is the question, we'll often get from investors, and frankly, I've asked on investor calls as well. Why hasn't every study in lung started yet? And I can sense that your team has been consistently very diligent and you've mentioned data-driven, I think that's right.

But there's a dynamic on this, which I don't think is well appreciated, which is pembro in lung may actually end up having a much more diversified revenue stream than I think people appreciate. People think about KEYNOTE-189 as a massive driver, but you guys have run adjuvant studies and maintenance studies. And so, this idea that frontline lung in that traditional sense is the be-all, end-all may not actually

end up being the case. Could you give some color on that in terms of when we think about pembro's revenue drivers today in lung, how diversified is it in the United States?

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

I am not the best person to speak to this, so I apologize already, but I should have these numbers and graphics and I do not. It is not the number one revenue generator for Merck. I can't speak to where that comes from, but you're right. We now have multiple studies in the adjuvant setting, including six that have overall survival. And more of the revenue, particularly future-looking revenue coming from KEYTRUDA QLEX. We anticipate in those settings. Less so in the 189 regimen.

Akash Tewari - *Jefferies LLC - Analyst*

Understood. Now, maybe going into ASCO, and I'd love to give -- you know, you obviously have a PD-1 VEGF in development that's Phase 3 ready. And your team has been very prudent in terms of where you want to develop that asset. But I'd love to get your take, as you've said, we want to get more data from the field externally before we figure out our own development program.

Obviously, we've got some important data sets from HARMONi-6, the ROSETTA data from BioNTech, and then also the lack of a PFS hit on HARMONi-3. How is Merck's view on where PD-1 VEGFs fit a role, particularly in lung, change post-ASCO?

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

This is such an interesting development for all of us as we think about how to optimize therapy for people with different kinds of malignancies. Through the KEYTRUDA program, we have more than 20 studies that we have done with different combinations of KEYTRUDA with VEGF inhibitors, including bevacizumab, where we have two approvals, Lenvatinib where we've seen some compelling data in endometrial cancer, as well as in renal cell, other VEGF TKIs. And so we've learned a great deal about the combinations over time.

And historically, it's not been a one-size-fits-all approach for these kinds of combinations. And what has really been the question, and I think people are more excited after ASCO is could the bispecific of putting these two together and potentially improving the therapeutic index by putting them together because the safety appears to be a little more tolerable, and maybe you can increase the efficacy actually of the PD-1 as well by the structure. Is that going to be what it takes to open up VEGF more broadly across multiple tumor types?

And I think we're still left with more questions than answers. So HARMONi-6 was great data. I want to congratulate Akeso, the investigators. It is clinically compelling information. It's the first Phase 3 randomized data set we've seen with the bispecific that shows consistency between PFS and OS.

But open questions remain regarding the translatability into global studies, the translatability into different subsets of non-small cell lung cancer, referring back to what you said with even look at HARMONi, and you look at HARMONi-2, where you didn't necessarily see that same correlation between PFS and OS.

There are also open questions about -- in that particular HARMONi-6 study about the differences in age that was seen, where you saw most of the benefit for those people who were less than 65. In a different magnitude, people keep talking about 407, KEYNOTE-407, and I'd like to point out that that study, the control arm, there was 60% crossover.

I don't know if people remember that 60% of the control arm crossed over to pembrolizumab. And the age hazard ratios, there was a small difference, definitely between those who were less than 65 and those who were older, but the magnitude of difference was not the same that was seen in HARMONi-6.

And so I'm excited because the curve separated and they stayed separated. Will they continue that way? I don't know the answer to that. When we look at the HARMONi, the HARMONi-2, they didn't seem to do that from the data we know to date. So I'm curious and it's an area where we want to continue to develop and explore, but how these agents will combine in different tumor types is to be determined.

So we're always, as you said, we're data-driven, we're very disciplined, and we will go where there's opportunity where we think the science and the clinical need makes sense.

Akash Tewari - *Jefferies LLC - Analyst*

Great answer. And there's a few threads I want to kind of pull on. I mean, A, you mentioned in 407, because I think there is this perception, well, squamous is slightly easier than nonsquamous, but you mentioned there's a lot of -- there was actually a lot of crossover in the 407 study. So maybe just generally this idea that pembro-chemo in nonsquamous versus pembro-chemo in squamous, there's a difference in terms of how difficult it would be to beat that regimen. It sounds like you're saying that's not actually the case. Both are going to be equally difficult to surpass. Is that maybe the right?

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

I think that people, KEYNOTE-189 has set a really high bar, and that's great news for patients. It set a very high bar.

And the other thing that we know is over time clinicians get better and better at keeping people on therapies as they learn how to identify who best benefits from treatment, how to modulate side effects, so dose intensity gets better. It's doing a really good job for patients. There's still a huge unmet need, so you want to develop things. I don't know that I would say that it's the bar is different as a barriered entry for squamous versus nonsquamous. They're different biologic subtypes.

Generally, the effects are somewhat similar for a checkpoint inhibitor between the two histologies. There's huge meta-analyses. There are more neoantigens in squamous, and so you might get a little more robust response there. So that may be what you're saying with area of entry?

Akash Tewari - *Jefferies LLC - Analyst*

Yeah.

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

The other aspect is that nonsquamous, there's more division of that histology into subgroups, such as RAS mutations are more present in those who have adenocarcinomas. And so it's more about how does the biology and the current therapy and thinking where the future is going. How then do you want to develop in these different spaces? And so again, we still have more questions than we actually have answers at this time.

Akash Tewari - *Jefferies LLC - Analyst*

Understood. Now, one of the data sets that I think I sense is going to be incredibly important, I'm curious if you share the view, is I think, Kelun has an 06 trial with sac-TMT and less than 1 percent NSCLC. You got the 1 percent to 49 percent data from 05 and my view was it did look incredibly strong, but it sounds like the less than 1 percent is an important part of that puzzle. Why is that, right? Why -- what are you going to learn from that 06 trial and you're hoping to see with sac-TMT in NSCLC?

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

There are a couple of questions there. The first question is related to does the PD-L1 expression level have any influence on the activity of sac-TMT? And there's not a biologic reason to expect that to happen. I think it's when you look at high PD-L1 expression tumor scores, the KEYTRUDA does better and better and other checkpoint inhibitors improve their activity as you get higher PD-L1 expression.

And so the bar to beat and improve upon that's higher, so the magnitude of benefit tends to be a little bit less.

The question that is going to come from this is related to can you increase the benefit of a combination there where people do use KEYTRUDA for the less than 1 percent but it's not uniform. And we have a lot of data showing that there is benefit in this population. So can you enhance that from an ADC combination? I think that's one of the questions.

We've seen some suggestions --

Akash Tewari - *Jefferies LLC - Analyst*

Really interesting.

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

For triple negative breast cancer that that could happen, that using an antibody drug conjugate, we've seen it in bladder cancer as well With a different antibody drug conjugate class. And so that to me is the question that I'm most curious about is, do you think that you can get something that is at least additive, if not better, by that combination? And that's what I'm hoping to see in that study.

Akash Tewari - *Jefferies LLC - Analyst*

That is a fascinating answer. Because I will say, even talking to Kelun, they strongly believe that there is an inherent synergy between pembro and sac-TMT.

And then there's also this dynamic of versus just traditional chemotherapy, you have a better durability of effect. So that's quite interesting. Which kind of leads me to another perspective, which is, KEYNOTE-189 was such a transformative trial because not only did you give great patient outcomes, but it was also the simplicity. I mean, there's no QCS, there's no TMB. This is something that every doctor, it's histology, people understand this and it can get used. And you've talked about this concept of workhorse regimens.

What's interesting to me is when I look at the OptiTROP-Lung05 data, I see a consistency of response. When I asked you about, less than 1 percent you're saying, I hope I see a consistency of response. And when I even look at the development strategy you had with Kelun, a lot of times you ran studies in subpopulations, but you're ultimately actually running trials pretty much everywhere.

So to me, the read is actually, we went conservative, but then we're seeing this drug is actually working more broadly. So that brings me to ultimately what your strategy could be in lung. Could it be that it's not separate trials in different sub-cohorts, but it actually could be another KEYNOTE-189 regimen where whether it's a PD-1 VEGF or pembro, that you could have a broad-based improvement across lines of therapy. And that's really ultimately where this is headed. I'm curious.

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

When we started the global program with sac-TMT. We tried to think ahead through three to five years from starting these Phase 3s. What was the therapeutic landscape going to look like? What was the clinical unmet need? And where can we add the greatest value? And that explains where we are today.

So for those who normally get pembrolizumab as a monotherapy, often these are older people who are not healthy. You don't want to give them chemotherapy for very specific reasons. sac-TMT is a cytotoxic therapy. It's an antibody for a conjugate, but it still has cytotoxic activity. So can you improve the efficacy because people unfortunately relapse and die in that population because they have metastatic disease, and so can that help? So that's that study.

The KEYNOTE-189 regimen, when you look at, you've got people who have squamous carcinoma and the biggest unmet need we saw was for a maintenance approach there. There isn't a maintenance therapy. There are different ways you could consider that population. It was you could add onto chemotherapy and KEYTRUDA and often you compromise on the chemotherapy dose or the antibody-direct conjugate dose or both where the benefit is probably from the maintenance approach and that also can make it more tolerable. So we think sac-TMT is a tolerable regimen that could be given for long periods of time in combination with KEYTRUDA.

And then when you think about the adenocarcinoma population, we were thinking ahead. We knew that RAS was coming into this space. That segment is getting more and more subdivided. I think that the data from OptiTROP-Lung05 and then, like you said, for 06 does raise the question of, is there the possibility that you will see some kind of sac-TMT combination across all of these subgroups?

And so we don't have studies that we've talked about fully in all of the different populations, but I think we've got a very diverse portfolio and you can look at the data from ASCO and you can make your own estimates about what we might do there.

Akash Tewari - *Jefferies LLC - Analyst*

Understood. Maybe just ending on sac-TMT and you mentioned something that I think is incredibly important is it's a tolerable drug. And one of the things that I noticed with the 05 data was that the duration on treatment, which is to me incredibly important, was double that of pembro monotherapy, which is unusual. Usually you wouldn't think the more cytotoxic combo regimen has that.

So a couple of things. Can you talk about really how you optimize the dose of Sac-TMT and Kelun, to their credit too, when they started at five and five and a half to then going to four, which seems like a Goldilocks dose. How you guys have learned to keep patients on therapy? how much of an improvement have you seen even from the early studies with sac-TMT to now the trials are running now? And how you expect that to translate into your own global Phase 3s? Should we expect this durability of response to carry out that might actually be even better than some of the early trials we've seen out of China?

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

There's a lot wrapped up in that question. So let me think about how to approach this. From the dosing perspective, antibody drug conjugates, they do have cytotoxic payloads. And so there is usually a dose response you see with chemotherapy. And so you do see this with sac-TMT is that the higher the dose, you tend to get increased efficacy.

You also get increasing toxicity too. So we're trying to look for that best optimal activity versus tolerability when we were choosing doses. We also wanted to have one dose for combination as well as monotherapy. And we have multiple studies where we're using sac-TMT as maintenance.

And so going with the highest dose that is tolerable doesn't always make sense in combinations because combinations increase toxicity. They always do. Whether it's a KEYTRUDA combination or any other kind of combination, side effects get worse.

And the PK between 5 milligrams per kilogram and 4 milligrams per kilogram heavily overlap. And so it's the totality of that, and we see very consistent sort of durations of response, PFS, and in the Phase 1 and Phase 2 data sets that led us to choosing this. And that's why you saw 4 milligrams per kilogram combined with pembrolizumab in the OptiTROP-Lung05 study.

So that's how we ended up with the dosing regimen that we did. And so thinking about this as am I could call it a workhorse environment called a cornerstone agency, is that for the clinicians out there, having one dose as modern combination makes their lives a lot easier. It really does. And so that way you don't have to think about it. It's in your pathways. You don't have to really question it. You just can prescribe it.

The AE management, I talked about this in regards to 189. Doctors get better managing toxicities over time. Whether the opportunity we had here with our partnership with Kelun is they were running studies ahead of us. And so we could learn from what they were doing.

So an example of this is stomatitis care. TROP2 is expressed in the intestine. All of the TROP2 ADCs have some GI toxicity. And for an example, in the Kelun studies, they do not routinely use steroid mouthwashes. We use them in our Phase 3 data sets. And we have increased the use of it.

We also use much more aggressive secondary growth factor prophylaxis because of the hematologic toxicity. And it also helps recovery of the intestine. And so we've been much more prescriptive about that. And these are AE management that oncologists are very used to giving in their daily practice and don't add significant burden to patients. If you're able to make the experience tolerable, then that's where you get the benefit.

How this will translate in global studies is to be determined. Global studies inherently are different than single region studies, whether they're China studies or a US only study. There's going to be variability there. And so we are teaching physicians in real time as they are getting used to these drugs. And so my hope is we have learned a great deal, thanks to our partnership and our very large Phase 1/2 program that we've done to date and we continue to iterate and evolve what we're doing in Phase 3 programs.

I'm encouraged by the endometrial readout, which you haven't seen the data yet. I have. Very exciting.

And so, you're having positive PFS and OS as the first ADC in a Phase 3 data set endometrial, I think supports that we're on the right path.

Akash Tewari - *Jefferies LLC - Analyst*

Understood. Now, last one on just speeding PD-1 VEGF and then I actually want to go broader. LaNova asset, I think the term Merck adopted was we're Phase 3 ready at ASCO. I will say the one question I think I've certainly thought of and I've heard this from investors as well is like it's unusual for Merck to present unconfirmed responses. I mean, you guys are very straight and narrow. You give confirmed responses, you give proper durability.

And at AACR, I think both in the poster and in the abstract, it was the same data cutoff. And so the question I've always had is really how did that data mature over time, really encouraging 55% response rate, but it was unconfirmed. Is there any qualitative color you can give us in terms of as you've given that therapy for a longer duration because that's really what you have internally, how that profile has evolved over time?

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

Yeah. I don't like to talk about data that's not public yet in any kind of forum. And so we have confidence in the data that we presented. Otherwise you wouldn't have seen us present information like that. And also we wouldn't call an asset Phase 3 ready unless we thought that what you would see is what you would get.

Akash Tewari - *Jefferies LLC - Analyst*

Understood. That's helpful in itself.

Now maybe stepping back and hitting on also CML and you guys just did some external BD there. I was happy, actually, I covered Terns. So that was great. But there's been -- I think, to me, it has been kind of frustrating because there's this idea like, oh, I read the deal documents and the response rate changed and this is not the asset we think it is. And I'd love to give you an opportunity to kind of, what is your perspective when you saw this 701 molecule in terms of A, safety and durability of response, but B, I really want to hit on efficacy, right?

I remember talking with Amy at Terns and she was saying we have the opportunity to maybe run a head-to-head study against Scemblix or run a study -- where we feel like we could be superior against standard of care, which is something Scemblix never showed.

So specifically on the efficacy front, what is your view of that molecule and what it can deliver?

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

We're really excited about the acquisition of Terns and TERN-701, which I think we've now renamed MK-4208, but we're calling it 7013. And this drug, we really appreciated that we think that they have improved the therapeutic index. And that's -- it's the way that they have presented data is very consistent.

When you look back, the original Scemblix Phase 2 datasets and Phase 1 datasets and the other second generation TKIs, they use the same terminology. So that way it was an apples and apples and directed the data set.

So that's where the dataset is. We were able in diligence to look at patient level data and look at every single patient including the ones that weren't presented at ASH last year and look broader. And so when we made the statements that the efficacy, you got incredibly fast kinetics of time to response.

We were able to independently verify and look at each patient and verify that. When we say that MMR is around 2 times what you would expect to see from more recent assets, we verify that information. And DMR 2 to 3 times, similar direct comparisons, again, all the caveats and limitations there. All of that is very accurate information.

And so we think this is something that does have the opportunity, as Amy had said when she was CEO of the company of being able to really improve outcomes. Not only in this relapse refractory population where it's originally studied, but I think a lot about the first line setting because clinicians still worry. Thankfully, the transformation in acute leukemia has dropped dramatically. And so it's less than about 10% right now. It's really come down.

But what you want to see is that very fast response. They do get better over time. I think there was updated data presented at ASCO of Scemblix that's showing over time things get better. But you really want that deep response, and then you want the durability of it because it opens up the potential -- for potential for some people to go off therapy. And this is a chronic disease, and after several years of therapy, if you keep someone very suppressed, you might be able to stop their therapy and give them a break.

This goes into the tolerability as well, is that most of the significant toxicities that have been reported with this class have occurred in the first six months. And so I think that that's definitely there are class effect, side effects that you are going to see that all of them are going to have. But it's the magnitude of them, the frequency and how you manage it that improves that therapeutic index. I think Terns has done a really nice job there.

So we're excited. We're continuing on with the program of progress. We're about a month into the acquisition and the integration. And we really are excited about the potential opportunity in the future with this asset.

Akash Tewari - *Jefferies LLC - Analyst*

Understood. And maybe just final point on that.

In terms of the design, I know it's early, in terms of Phase 3, I think you're quite important about deep molecular response and that could be curative. Could you run head-to-head studies? Could you run or a trial where it's more traditional to what Scemblix said, which is kind of frontline against standard of care?

Is there a discussion internally for your team to take the more aggressive approach or it will be more traditional?

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

We're still a month in, so give us a little time.

Akash Tewari - *Jefferies LLC - Analyst*

That makes sense. Now maybe stepping back, the ADCs you don't get asked a lot about are the Daiichi ones, and that at the time --

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

That's sad because they're great.

Akash Tewari - *Jefferies LLC - Analyst*

Okay. So, and that's incredibly important because, again, one of the largest pharma partnerships ever, I think probably the largest at the time of the deal, but, I think there's been mixed headlines, it's a really competitive landscape, and there's always this question of, well, which one of these assets is Merck right now most excited about?

I'd love to give you a chance to refresh in terms of the data that you have internally because you're running these dynamic Phase 2/3 trials, larger Phase 2 studies. So there's a lot of data given internally that maybe is not public yet. Of the three assets, which one do you feel like since you've acquired it, you've gotten much more excited about as you've gotten more clinical data?

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

This is always hard because it's like asking what your favorite child is or what is it that you like to do?

The IR team will laugh because if I get asked a question, I always like to mention one specific drug is my favorite drug. A, because they're also different and special. They -- each have fantastic potential. And that's what I think is that -- we saw that initially when we did the diligence and we start our initial discussions. And as we're seeing data come out, if you look at I-DXd, we've got a PDUFA date in October for small cell lung cancer where there's tremendous of that need about 4 percent survival at five years for this horrible malignancy and very compelling efficacy from the Phase 2 data set. We have ongoing Phase 3 study and potential for combinations also with MK-6070, which is our DLL3.

We have ongoing Phase 3 studies looking at I-DXd and esophageal cancer as well as in prostate cancer, which they're all exciting to me. And I think, the continued data that we're seeing keeps me excited about that asset and potential. We have other Phase 2 studies ongoing which we've not publicly disclosed.

If I move to R-DXd, another one where it's, again, exciting and compelling data. It is -- you see very marked responses in platinum resistant to ovarian cancer. So we have Phase 3 studies ongoing in the platinum resistant setting. We have large Phase 2 data sets and more Phase 3s soon to follow in this indication.

We are also looking at R-DXd and other tumor types, and so we're waiting for emerging data to help inform where else this drug could potentially go.

And then with P-DXd, we started a Phase 3 in breast cancer. And so HER3 is really important in breast cancer in a way that I think is not always appreciated. And so we started one in hormone receptor positive breast cancer, including a combination with KEYTRUDA, where normally you don't give KEYTRUDA. And it's partly what you mentioned earlier about the ADC combination. Can it improve the likelihood of benefits to a checkpoint inhibitor because of increased antigen exposure? Is there something there that makes that happen?

And with this. Also, in the study, in HER2 is allowed in the control arm because it does have very, very low HER2 levels in there, and we know that there is expression response with the ADCs generally across the Board.

We also are doing Phase 2 studies, and this is public information, looking at HER2 positive because HER3 is particularly important in HER2 positive disease, and HER2 has done an amazing job. I'm a former Breast Oncologist, now a drug developer, and for me as a breast oncologist, HER2 has been transformative. And HER2 positive disease, but there's still a ton of them that need, and people diagnosed with de novo breast cancer, so opportunities for multiple different kinds of combinations to innovate there.

Akash Tewari - *Jefferies LLC - Analyst*

And a quick point on that, de novo. I mean, this question, I think Lilly presented some data with Nectin-4, and to me, this is like -- this is a huge problem. You have all these topo ADCs, they're all going frontline, you're going to have this issue in ovarian. And I think there is early signs that if you retreated with topo. You're not getting a response at all, regardless of even changing the target.

So when you talk about HER3 for breast, is that -- what's your confidence that you can retreat with the topo toxin and get a response? Or is it more, we're trying to go to populations where HER2 really hasn't gone?

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

I think it's to be determined. And so there are multiple different data sets. It's -- well, if I take a step back and just talk about chemotherapy, and so I'll go back to my history as a Breast Oncologist. We would never treat someone with paclitaxel to go to docetaxel. We would never treat someone with Adriamycin and go to Doxil. You don't do them sequentially like that.

And so there have been data sets presented that have shown that if you do ADC-A with the topo to ADC-B with the topo, you don't see a lot of activity. That doesn't surprise me. The big question is at what treatment-free interval do you get sensitivity back and does that happen? Because you can retreat with taxane from breast cancer if you have a period of time between them and get quite robust activities. Same thing's true with anthracyclines. You can retreat with Doxil if you've had Adriamycin and get quite robust activity.

So I think it's to be determined. If the mechanisms of resistance are different, with the topos, you can get topoisomerase I mutations, and you also can get change in efflux pumps. And probably it may be that specific topo payload that could make a difference on whether or not there's response to.

So a lot for us to learn and think about moving forward.

Akash Tewari - *Jefferies LLC - Analyst*

Understood. I have a little break on my next meeting, so I'm selfishly going to ask one more question. She's giving me a scowl, but it's fine.

On the Moderna-INT partnership, and I say this is, I'm probably, I was more skeptical than anyone else. I was like, oh, there's all these LAG-3 studies in adjuvant, and they've all failed, actually. And you continue to present really interesting data regardless of PD-1 expression of a

durable response, which I think is quite interesting. I want you to talk about the signal you've seen in melanoma and how it might apply to lung. Has you -- has your confidence in that program increased and what are you learning about the biology of these personalized cancer vaccines that maybe we don't appreciate?

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

So for those who are not familiar, 942 is a study looking in Stage II and III melanoma. Pembrolizumab versus pembrolizumab combined with INT five-year follow-up information. You saw that there is almost a 50% reduction of distant metastasis as well as relapse-free survival. So I'm rounding up one number, rounding down another number.

So really compelling activity that's prolonged. They also had exploratory data showing T-cell clonal expansion that was maintained even though the INT was stopped. And it wasn't continued on, no boosters were given.

So the question that you're asking is how do we take that and apply it to non-small cell lung cancer? The reason why we started Phase 3 is we just opened up one in Stage I lung cancer, non-small cell lung cancer, relates to the TMB levels and the neoantigens, the similarities that you see between non-small cell lung cancer and melanoma, the underlying biology of what makes something immunosensitive is the most similar between these two diseases, which is why we started our Phase 3 programs.

We have multiple Phase 2 studies looking more broadly. For example, renal cell, which is IO sensitive, has less neoantigens. And so will something like INT be effective there? And then other studies which are IO sensitive, like bladder cancer, we have Phase 2 studies ongoing to really understand that as well. So more to follow --

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Akash Tewari - *Jefferies LLC - Analyst*

More to follow indeed. Thank you.
