Folks, welcome to Yale Cancer Center, Grand Rounds. I’m Kevin Billingsley, and I have the pleasure of welcoming our visiting speaker today. Doctor Charles Balch is, no exaggeration, a giant of multidisciplinary cancer care and surgical oncology. We’re thrilled to have him here today. Doctor Balch is a professor of Surgical Oncology in the past chair of the Department of Surgical Oncology at the UTMD Anderson Cancer Center.
He has had an extensive and distinguished career as both a clinical and academic surgical oncologist, and he's one of the leading authorities in both Melanoma and Breast Cancer Care. Over the course of his career, Doctor Balsh has made significant contributions to laboratory research in tumor immunology and human T lymphocyte differentiation. He started his medical career in Med school at Columbia, where he and then he went on to surgical training at both Duke and the University of Alabama, followed by additional laboratory work.
experience with an immunology fellowship at the Scripps Clinic, which clearly laid the groundwork for his Seminole contributions in tumor immunology and Melanoma.

He’s the founding Editor in Chief of the Analysis Surgical Oncology and Editor in Chief for the Patient Resource Cancer Guides, which are distributed to over 1,000,000 patients every year.

Doctor Balch has had an extensive history of prominent leadership roles in multiple centers across the country. He served as the Executive
Vice President and CEO of ASCO.

He's also served as the President and CEO of the City of Hope National Medical Center, as well as the Chair of Surgery at MD Anderson.

Over the course of his career, he's accumulated over 700 publications across a variety of areas in research and clinical practice.

And one of the things that in my conversations with him, he and I have truly connected on are the importance of leadership and community building around multidisciplinary cancer care and care coordination.
So one of the things that I think I have taken away from my conversations with him that I’m sure he will be sharing today is the importance and our ability as oncologists to serve our patients and our communities and a variety of ways. And he’s really shown how all of us can do this over the course of our careers, both through our direct clinical care, through education, through mentorship, through research, both clinical translational and basic science, and...
through leadership and patient advocacy.
So today, he will be speaking on the role of surgery after neoadjuvant systemic therapy.
And it is a real pleasure to have you here, Doctor Balch.
Thank you.
Well, thank you, Kevin,
Bill and Sleep for a wonderful introduction and I’m honored to be here with all of you today.
So there are many themes we could talk about because we are now in a revolution of oncology care.
Profound changes are occurring now and I thought what would be
Important today is a theme to talk about how the field of surgery and surgical oncology is going to have to change and adopt to the new advances in molecular profile diagnosis in systemic therapies, in immunotherapy and the changes we are going to have to adopt to. So for some of you might say that’s not what I’m doing in my practice today, but I can almost guarantee you within the next 5 to 10 years, everybody in this room who is a surgeon is going to be impacted by the things that we’re showing today.
And so as I go over some of these themes, I’d like you to think about the strategies that work in one tumor area, but understand that these are common to our understanding about the management of other cancers as well. That’s particularly true in the immunotherapy field. So I’ve presented examples that I think are larger strategies that apply to our cancer care delivery system that is now being almost exclusively multidisciplinary. There are very few circumstances now where one modality in solid tumors will treat the patient anymore.
So let me go over this.

This is flying above the trees.

Think about the strategies, not the details on the slides.

And there are many things I can’t cover in the time allowed that we can take for questions later on if necessary.

So we’re should I use this?

Yeah, you can advance with the keyboard if you want. OK. All right. Well, let me start out with just the key messages of what I’m going to present as examples over time, so that you can focus on the strategies.
of this talk is that surgery will not be the first treatment for most cancers except for stage 1 cancers. That’s a revolutionary change. Where heretofore the patients usually went to the surgeon first who then kind of coordinated the care. But now because of these advances in systemic therapy, surgery will not be the first and we need to be part of a multidisciplinary team and we must emphasize that be involved in multidisciplinary treatment plans because each of us bring to the decision making a different perspective based upon our training and so forth.
And it’s the collective wisdom of the different oncology specialists that is really what’s best for the patient. So all of us treating cancer in a specific disease need to be together and collectively decide on the best treatment plan for a patient, what’s the right combination and sequence that involves all of our modalities. And that as I’ll show you that the standard of care, what we called neoadjuvant surgery, think our medical colleagues are beginning to talk about neoadjuvant surgery, that the primary treatment is systemic now,
but it doesn’t make a difference in the term.

But what we call neoadjuvant therapy is now becoming the standard of care for many, if not most cancers. And this is an area based upon clinical trials that is showing value in almost every cancer where it’s tested. There’s sure there’s a few that are resisted, but if you think about the future and the advances we’re making, this will be a common element of our treatment that the first treatment will not be surgery, it will be a systemic treatment. And I’ll go over with you about the value of that to the patient in
their management. The other part of this is that immunotherapy now is the established 4th modality of cancer. But I want to emphasize as I get to the slide, this is a totally different treatment and the standard chemotherapy, targeted therapy, endocrine therapy that directly treats the cancer immunotherapy, these checkpoint inhibitors do not treat cancer and that has to be the first part of the logic because we can’t use the rules of chemotherapy.
When we applied to immunotherapy, it’s a different process and we’re treating a dysfunctional immune system that is common to most cancers. So the other emphasis on this because there’s some emphasis, well, maybe we don’t need surgery anymore, but I would argue that surgery is going to be incredibly important for staging, as I’ll show you as a reliable means of staging the tumor response and giving to the pathologists not only whether there’s a complete response, but the residual tumor burden is now an important prognostic factor that is going to dictate our subsequent treatment.
And then because of these advances in systemic therapy that surgeons will no longer be performing the radical operations that we did in the past because that was all that was available for many cancers. And so we’ll be doing de-escalation much more conservative tissue sparing, organs sparing operations and even if, as I’ll show you in three different cancers in our future watch and wait that we will not do surgery, we’ll follow the patients. And then there’s going to be a whole new lexicon that will need to do much.
more research on salvage surgery.

Which patients can we select not to do surgery?

How often do we follow them?

What operation do we do when they relapse?

And can we do this without compromising their survival by not doing an operation at the outset.

And I'll show you three different examples.

And then for those of you who are in training that in all of us who are in practice, the field is moving fast in both the continuing education through organizations like ASCO.

And in our training we need to have surgeons who are trained in oncology.
And as Kevin Billingsley and I've talked about, I really present myself because the way I think is I'm an oncologist who operates because oncology deals with the chronic condition of cancer, whereas surgery deals with the episode of the perioperative period. But once the patient’s wounds have healed, they’re still an obligation for us as surgical oncologist to continue being involved in the long term management of the patient. So that’s the summary of what I’m going to talk about.
I do want to just take a moment to say I predicted this 30 years ago in my presidential address in at the SSO, and I wanted to point out what I said, 'cause this was about surgical oncology in the 21st century. And I said that in the 21st century, only a minority of patients with cancer will have surgery alone as a single modality. And it’s more likely that chemotherapy and even radiation therapy will be the initial treatment for many patients, while surgical treatment for some types of cancer will be relegated to a secondary or tertiary level. That was 30 years ago.
And that prediction now is really valid for most types of solid tumors. So why is that? Because we’re now in a new pathology with molecular diagnostics in this slide, showed the old way with these which is just a cartoon, showed the old way with these general diagnosis of solid tumors, we gave our therapy and hope that 10% of the patients might respond and we declared that as a victory. But now with genomic analysis, we select patients based upon their specific mutational events and other factors. And now as you’ll see,
instead of getting 10% response rates,
we're talking about 50 to 70% pathological complete responses based upon the selection of the patients and these new agents that are so much more effective. So as I mentioned, the advent of various immunotherapies because we now have discovered which is different than all of our strategies beforehand where we assumed the immune system was deficient and we gave various forms of immune stimulants which didn’t work. So now we are discovered that in most human cancers that have survived in our patients,
00:13:10.517 --> 00:13:13.105 of their tumor antigen and inducing
00:13:13.105 --> 00:13:16.087 tolerance so that no matter how much
00:13:16.164 --> 00:13:19.076 you try to stimulate the immune system,
00:13:19.080 --> 00:13:21.055 it can’t respond because it’s
00:13:22.640 --> 00:13:24.453 This is no different than if you
00:13:24.453 --> 00:13:26.307 were allergic to grass and you go
00:13:26.307 --> 00:13:28.456 to the allergist, what do they do?
00:13:28.456 --> 00:13:31.180 They inject low doses of grass so that
00:13:31.180 --> 00:13:33.160 regardless of your exposure to grass,
00:13:33.160 --> 00:13:35.512 your immune system does not recognize
00:13:35.512 --> 00:13:39.678 it as not self and does not react to it.
00:13:39.680 --> 00:13:41.976 And so I think we’ve learned now
00:13:41.976 --> 00:13:44.500 that for many human tumors and we’re
00:13:44.500 --> 00:13:46.040 still sorting through this,
but it is revolutionary as a discovery

that the main reason that tumors have

survived in patients we see clinically

is because they have blindfolded the

immune system into a tolerant state.

So if we can unblindfold the immune system,

we then have a personalized treatment

that reacts against the specific array of

tumor antigens in each individual patients.

So if tolerance is broken now,

then the immune system can

reject the foreign invaders.

And of course,

there’s a price for that when we’re

doing something profound by breaking

the spillover is
breaking tolerance to self antigens.
And so if you look at the array of complications we have with immunotherapy, you can explain them all as a form of autoimmunity.
And that the good news is that we could treat autoimmune diseases with Prednisone and taper. Those over time reverse the toxicity.
And interestingly, in contrast to chemotherapy, you can go back to the same immunotherapy in these patients and surprisingly they don’t enter into toxicity the way they did the first time around.
So there’s a lot we have to learn about this. And when I wanted to point out if course, as you know that Jim Allison and to Soko Hanjo received the Nobel Prize for this. But I think another person who profoundly influenced the field that I wanted to give a shout out is here at Yale. And that’s my friend who I worked with, Li Ping Chen, when he was at Hopkins and we were working on Melanoma immunotherapy. He was the first to specifically state that a monoclonal antibody against...
B7H1 would break tolerance in a mouse model and therefore be an effective therapeutic strategy for cancers. And Leipeng worked with a group of us, This is Li Ping and Suzanne Tipalian, who I helped recruit to the surgery department at Hopkins, and her husband, Drew Pardo, who is the chair of immunology. So this is an example of translational research in the collaboration with clinical scientists. So Li Ping’s research directly stimulated Drew and Suzanne to take out a seed culture they had.
frozen to do a phase one study.

They grew up this monoclonal antibody.

Mike Carducci at Hopkins, the phase one director gave it to a young person as an assistant professor named Julie Bramer, who is a pulmonary oncologist.

And our recommendations was that you use renal cell and Melanoma to test this new drug because everybody knows that’s the only diseases that work.

But Julie came in one day at our Friday meeting said you won’t believe this, but my lung cancer patients are responding to this new drug.
So BMS swooped in, bought the biotech company that had done the seed culture and that became the volume up. But it’s a great example of collaboration between clinical and laboratory scientists that led directly to a major advance in cancer treatment. And I use this. This is an unusual example, but it shows the power of the immune system. This is a grapefruit sized Melanoma that was treated with a single dose of nivolumab and epilumab with a complete destruction of that tumor.
That’s APCR after one treatment.

And I use that only as an example to show you the power of the immune system when you take the blindfolds off, when you break tolerance. And that’s unusual to have this, but as I’ll show you, it’s not uncommon either.

So now there are 9 powerful checkpoint inhibitors with different mechanisms of action. And as we know with drugs that combined drugs with different mechanisms action, we can get an additive effect. So now we’re showing that the
NOTE Confidence: 0.802761662
00:18:09.712 --> 00:18:12.462 combinations of anti CTLA 4 which
NOTE Confidence: 0.802761662
00:18:12.462 --> 00:18:14.994 works in the central lymphoid section
NOTE Confidence: 0.802761662
00:18:15.000 --> 00:18:18.288 and either anti PD one or PDL one
NOTE Confidence: 0.802761662
00:18:18.288 --> 00:18:22.101 which works in the periphery that they
NOTE Confidence: 0.802761662
00:18:22.101 --> 00:18:25.080 combination is better than either alone.
NOTE Confidence: 0.802761662
00:18:25.080 --> 00:18:27.425 And this slide just shows you briefly
NOTE Confidence: 0.802761662
00:18:27.425 --> 00:18:30.008 in a cartoon that they’re now with
NOTE Confidence: 0.802761662
00:18:30.008 --> 00:18:32.264 different trade names but the same
NOTE Confidence: 0.802761662
00:18:32.331 --> 00:18:34.743 types of drugs working in this
NOTE Confidence: 0.802761662
00:18:34.743 --> 00:18:37.042 signaling pathway between PDL ONE and
NOTE Confidence: 0.802761662
00:18:37.042 --> 00:18:39.429 PD ONE and a separate mechanism of
NOTE Confidence: 0.802761662
00:18:39.429 --> 00:18:42.076 the first drug which was Ibilimed,
NOTE Confidence: 0.802761662
00:18:42.080 --> 00:18:45.090 which works in the central lymphoid tissue
NOTE Confidence: 0.802761662
00:18:45.090 --> 00:18:47.918 with a different mechanism of action.
NOTE Confidence: 0.802761662
00:18:47.920 --> 00:18:50.629 And now even after only 11 years
NOTE Confidence: 0.802761662
when the 1st paper was presented,

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I'll show you a slide in a minute.

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You can see where the FDA has approved as an indication the use of immunotherapy,

NOTE Confidence: 0.802761662

the same drug,

NOTE Confidence: 0.802761662

the same drug course.

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We're not treating cancer.

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We're treating a common deficit in most cancers that come alongside our traditional treatments to treat the patients with a variety of cancers.

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And every month there's new indications that are approved based upon what is now over 1000 clinical trials going over various drug doses and indications for immunotherapy.
So that those powerful drugs that were started out with advanced disease have now moved into the neoadjuvant space. And I want to show you the reason why that is valuable in neoadjuvant therapy. So from this wonderful paper from my colleagues at MD Anderson that the advantages are one that downstages tumors and increases the ease of surgical resection, including importantly the conversion of inoperable or borderline operable tumors into operable ones. Importantly, as I’ll show you...
00:20:06.880 --> 00:20:09.880 the pathological response is a surrogate
NOTE Confidence: 0.901970194736842
00:20:09.880 --> 00:20:12.600 endpoint for long term benefit.
NOTE Confidence: 0.901970194736842
00:20:12.600 --> 00:20:14.592 So we can find out if drugs work
NOTE Confidence: 0.901970194736842
00:20:14.592 --> 00:20:16.539 within six weeks instead of giving
NOTE Confidence: 0.901970194736842
00:20:16.539 --> 00:20:18.621 them after surgery and following the
NOTE Confidence: 0.901970194736842
00:20:18.687 --> 00:20:20.836 patient for five years and then going
NOTE Confidence: 0.901970194736842
00:20:20.836 --> 00:20:23.014 back and seeing how many survived.
NOTE Confidence: 0.901970194736842
00:20:23.014 --> 00:20:26.584 So doing this up front gives us a
NOTE Confidence: 0.901970194736842
00:20:26.584 --> 00:20:29.344 better indication early on based
NOTE Confidence: 0.901970194736842
00:20:29.344 --> 00:20:31.552 upon the pathological response.
NOTE Confidence: 0.901970194736842
00:20:31.560 --> 00:20:33.996 And what what you’ll see is the
NOTE Confidence: 0.901970194736842
00:20:33.996 --> 00:20:36.272 residual tumor burden is important
NOTE Confidence: 0.901970194736842
00:20:36.272 --> 00:20:39.124 now in a cancer management.
NOTE Confidence: 0.901970194736842
00:20:39.124 --> 00:20:42.638 It allows us to test novel combination
NOTE Confidence: 0.901970194736842
00:20:42.638 --> 00:20:44.528 strategies and investigational drugs
NOTE Confidence: 0.901970194736842
00:20:44.528 --> 00:20:47.580 because we can take out the tumor
after the exposure to these drugs and determine the new molecular profile of the cells that are refractory. And I’ll show you a classic clinical trial that she demonstrates that. And then the other reason is the improved responses are better than in patients with advanced burned metastatic disease where their previous chemotherapy itself is immunosuppressive and their volume of cancer itself provides an antigen excess which is immunosuppressive itself. So if we’re doing this up front, when there’s a smaller tumor burden,
you get a better immune response and then we have some molecular markers, the CPS score and and other markers, but we really need better and more precise markers to help select our patients. So these are just a partial example of successful neoadjuvant trials that have led to approved indication by the FDA. And my point is this is a range of cancers, this is a common abnormality to human cancers. And as we’re learning how to use these checkpoint inhibitors and various combinations and sequences, they’re adding to the advances of our cancer management not
as a substitute necessarily, but alongside is what I call the 4th modality of cancer treatment. So here’s another hypothesis that has been proposed that I’ll show you the results that led to a clinical trial. And as you could see in the upper cartoon that if the surgeon takes out the bulk of the tumor and leaves microscopic tumor left behind and gives immunotherapy, there’s not many cancer cells to stimulate the immune system. But on the other hand, if you give the immunotherapy up front, when there is a larger and more
00:22:46.119 --> 00:22:47.370 representative tumor burden
NOTE Confidence: 0.901970194736842
00:22:47.448 --> 00:22:49.360 and tumor antigen exposure,
NOTE Confidence: 0.901970194736842
00:22:49.360 --> 00:22:53.070 you will get a more robust and
NOTE Confidence: 0.901970194736842
00:22:53.070 --> 00:22:54.914 consistent immune response.
NOTE Confidence: 0.901970194736842
00:22:54.914 --> 00:22:58.199 And this is demonstrated amazingly
NOTE Confidence: 0.901970194736842
00:22:58.199 --> 00:23:01.644 in this randomized clinical trial
NOTE Confidence: 0.901970194736842
00:23:01.644 --> 00:23:04.396 which proves this hypothesis.
NOTE Confidence: 0.901970194736842
00:23:04.400 --> 00:23:07.354 In fact, I'm astonished at the results.
NOTE Confidence: 0.901970194736842
00:23:07.360 --> 00:23:10.580 So this randomized trial gave
NOTE Confidence: 0.901970194736842
00:23:10.580 --> 00:23:13.156 everybody with metastatic Melanoma
NOTE Confidence: 0.901970194736842
NOTE Confidence: 0.901970194736842
00:23:16.320 --> 00:23:19.757 Drug in this case was pembro Elizabeth.
NOTE Confidence: 0.909291
00:23:19.760 --> 00:23:22.895 And they were randomized
NOTE Confidence: 0.909291
00:23:22.895 --> 00:23:24.675 to receive 18 courses,
NOTE Confidence: 0.909291
00:23:24.680 --> 00:23:26.678 but half the group got three
NOTE Confidence: 0.909291
00:23:26.678 --> 00:23:28.552 courses up front and everybody

else got 18 courses afterwards.

So that was the only difference with this monotherapy.

We don’t use monotherapy anymore like this,

but look at the difference between those patients who had three courses of single agent immunotherapy

up front and those who didn’t,

which demonstrates what I just showed you in that hypothesis is the value in survival rates by giving checkpoint inhibitors before they’re to the bulk of their tumor is removed and this gives the rationale for neoadjuvant immunotherapy.
Another example that I want to show you from my colleague Merrick Ross. This is a Melanoma patient who presented with borderline operable bulky nodal metastasis in the groin and the pelvis. And this patient would have ordinarily had a radical dissection of the groin after immunotherapy, you can see that there is a down staging and the tumor size has decreased, so facilitating an operation. But it wouldn’t surprise you that when all the tumor was removed there was nothing left.

The masses that we’re seeing were
inflammation and scar tissue in a classic rejection response, the same as what you’d see with a transplanted organ or a viral infection. That the mass that we’re seeing on X-ray was not tumor anymore, it was scar and inflammatory tissue. So the key point here is we can’t gauge responses by X-ray verification. The surgeon needs to take it out, give it to the pathologist to determine the degree of response and to do a new molecular profile to look at the molecular profile of the refractory cells. So this was the first immunotherapy
00:25:30.056 --> 00:25:32.970 trial presented in the world 2010.
NOTE Confidence: 0.909291
00:25:32.970 --> 00:25:35.840 So this is a very new field.
NOTE Confidence: 0.909291
00:25:35.840 --> 00:25:38.096 This was using the maximum tolerated
NOTE Confidence: 0.909291
00:25:38.096 --> 00:25:40.925 dose of a single agent EPI LUMA Med
NOTE Confidence: 0.909291
00:25:40.925 --> 00:25:43.148 and of course the problem with this
NOTE Confidence: 0.909291
00:25:43.148 --> 00:25:45.154 although this became a standard of
NOTE Confidence: 0.909291
00:25:45.154 --> 00:25:47.320 treatment until we found out that
NOTE Confidence: 0.909291
00:25:47.320 --> 00:25:50.539 at that MTD that 50% of patients
NOTE Confidence: 0.909291
00:25:50.539 --> 00:25:53.570 had grade three grade 4 toxicity and
NOTE Confidence: 0.909291
00:25:53.659 --> 00:25:56.165 some patients died because of that.
NOTE Confidence: 0.909291
00:25:56.165 --> 00:25:59.000 It was also shown that as a single
NOTE Confidence: 0.909291
00:25:59.000 --> 00:26:01.478 agents it’s inferior to an anti
NOTE Confidence: 0.909291
00:26:01.480 --> 00:26:02.794 PD1 checkpoint inhibitor.
NOTE Confidence: 0.909291
00:26:02.794 --> 00:26:06.406 So in large part this drug was not
NOTE Confidence: 0.909291
00:26:06.406 --> 00:26:09.160 used anymore because of the toxicity.
NOTE Confidence: 0.909291
00:26:09.160 --> 00:26:09.627 However,
the teaching point here is you can’t treat immunotherapy agents like drugs and in fact a dose now of 1 to 3 milligrams which is not very toxic when added to another checkpoint inhibitor has an added benefit. So we have to get away from testing these some of these agents by their maximum tolerated doses when actually lower doses work just as well if not better and a more tolerable. So we’ll go over the details of this randomized study that looked at different dose schedules and doses of combining hippilumamid at 3kg and 1
milligrams with combinations of nivo.

And this Arm B, just to accelerate the talk,

turned out to be the most efficacious in the least

toxic. But here's the teaching point I wanted to make in this randomized study. This is the radiological response to patients being treated in this randomized study with metastatic Melanoma, mainly stage 3. And you can see there's a complete response radiologically in 10% of patients, a partial response in 50%. However, when the patients had surgery and the pathologist could examine it, you see the difference,
57% of those patients had APCR and 7% had a near PCR. So compare the difference between the radiologic response and what the pathologist found. You cannot look at these masses on X-rays and know what’s inside them because these tumors in many cases are replaced by inflammation and scar tissue. So the surgeon has to take them out and give the specimen to the pathologist. And as I’ll show you in tumor after tumor, the determination of PCR near PCR versus more residual tumor burden is now an important part of our cancer management.
But in my early days, giving interleukin interferons tumor cell vaccines, if we had a 5% PCR rate, that was a victory. If we had a 15% partial response, that was a victory. And as I told one person earlier, we tortured people with alpha interferon over many dose schedules in years because that’s all we had and we improved survival rates by 2%. So now in this new era of Melanoma management with the advent of immunotherapy because we still don’t have good chemotherapy, we have some targeted therapy.
Look at the pathological responses now that range in this study between 65 and 80% and pathological complete response in dose schedule BPCR in 57% of patients Never in the history of treating cancer have we seen these kind of dramatic responses. So this also shows you just in one other cartoon the value of combining two different checkpoint inhibitors which have different mechanisms of action. And if you look on the two pies charts, you can see that with an anti PD one you get a 20% PCR but if you add low doses of ipilumab you double that to 43%.
So again showing as we use with combination chemotherapy with different mechanisms of action, the new standard is using these combined checkpoint inhibitors. But the important point is the lower doses and shorter schedules work just as well as high doses given over a long time because what we're doing is like turning on and off switch, we're breaking tolerance. And I predict that we will not be giving a year of immunotherapy before we'll have to do the clinical studies to show that it's equally good of giving shorter courses.
So this is one of my first key points about the impact on surgery. This is a study by Prada going on now which is a randomized study but for which we have some of the early results. These are patients who present with stage 3B and 3C disease. They have clinically and radiologically detected nodal metastasis and index node has a marker placed in the largest lymph node. Then the patients get only two cycles of combination of immunotherapy, of which only two cycles and then that index node that’s all that is removed. And you can see the strategy those patients
who had APCR or near PCR less than 10%
00:31:00.880 --> 00:31:03.796 viable cells had no therapeutic lymph
00:31:03.796 --> 00:31:07.199 node dissection and no adjuvant therapy.
00:31:09.404 --> 00:31:12.159 APCR did get a therapeutic,
00:31:12.160 --> 00:31:14.290 no dissection and follow up and
00:31:14.290 --> 00:31:17.039 those that did not get a response
00:31:17.039 --> 00:31:19.553 had both a therapeutic lymph node
00:31:19.553 --> 00:31:21.960 dissection and adjuvant immunotherapy.
00:31:21.960 --> 00:31:24.725 But the point is that’s already been
00:31:24.725 --> 00:31:27.633 reported is that in the patients entered
00:31:27.633 --> 00:31:31.168 into this trial that 60% of them never
00:31:31.168 --> 00:31:34.000 needed a therapeutic lymph node dissection,
00:31:34.000 --> 00:31:37.240 which was their standard treatment before
00:31:37.240 --> 00:31:40.440 because they achieved APCR or near PCR.
00:31:40.440 --> 00:31:42.974 And I’ll show you more examples of
this and other diseases as well.

So let me move on to breast cancer and neoadjuvant therapy.

So there’s another principle here that if we don’t get a pathological complete response, you could predict that the residual tumors are going to be refractory to the drugs that you gave up front.

So why continue them afterwards when these refractory tumors probably have a different molecular profile in the strategy here which is a classic in that I think applies to other tumors as well was this Catherine study which took her two positive patients.
who got neoadjuvant treatment.

They all had residual invasive
disease after getting their standard,

her two therapy either single or dual

therapy targeted therapy and then we're

randomized to switch their treatment

if they had residual disease into a

different drug TDM one or continued

the same drug that they were on before.

And this study of course showed that

by switching therapies intuitively

this makes sense.

You get an improved survival rate in

those patients who we stopped after

six weeks and switched to another

therapy to treat the refractory
00:33:00.511 --> 00:33:03.195 tumors and that in turn increased survival rate in these patients.

00:33:03.195 --> 00:33:05.835 And this is going on in all the other subtypes of breast cancer.

00:33:05.840 --> 00:33:08.048 And my point here is you look at the residual tumor burden, which shown in the different colors the differences in survival rates over 8 years based upon the subtypes of breast cancer and how those patients who have APCR or new PCR do very well over 8 years.

00:33:12.025 --> 00:33:14.079 But in contrast, those patients who have more residual tumor burden obviously are going to
need a different therapy and have a worse prognosis if we continue to give the same treatment and don’t switch. And so now there are a number of clinical trials, I’m just showing one examples. It was showing that post neoadjuvant treatment options a different treatment than what was given up front but directed by the residual tumor burden cause can improve survival rates with a range of switching therapies. So the teaching point here is now we have enough agents we can go to second line therapy early based upon the residual tumor burden after the surgeon
00:34:15.187 --> 00:34:17.477 takes the area out where the tumor
00:34:17.477 --> 00:34:20.039 was and gives it to the pathologist.
00:34:20.040 --> 00:34:23.851 So here’s another important strategy is
00:34:23.851 --> 00:34:26.536 if we’re combining chemotherapy with
00:34:26.536 --> 00:34:28.894 immunotherapy that the chemotherapy that
00:34:28.894 --> 00:34:32.187 works directly on the tumor is going to
00:34:32.187 --> 00:34:34.515 break down the tumor into apoptosis.
00:34:34.520 --> 00:34:36.840 It will release tumor antigen
00:34:36.840 --> 00:34:39.199 and in so doing becomes a boost,
00:34:39.200 --> 00:34:41.444 an immunological boost or an internal
00:34:41.444 --> 00:34:44.190 vaccine if you will for the immune
00:34:44.190 --> 00:34:46.160 system where tolerance is broken.
00:34:46.160 --> 00:34:48.463 So it wouldn’t surprise you if you
00:34:48.463 --> 00:34:50.200 use these combinations you will
00:34:50.200 --> 00:34:51.238 get better responses.
And in these non randomized studies in the right you can see the PCR rates was 60% or more PCR by using a combination of neoadjuvant therapy in a series of trials, I'll just go over them quickly, the KEYNOTE 522 and the impassioned O31 using different checkpoint inhibitors combined with the same classic chemotherapy up front for 12 weeks and then randomizing the patients between checkpoint inhibitors or placebo. You can see in both of these trials that the PCR rate was higher in both trials by adding immunotherapy to chemotherapy is neoadjuvant therapy.
So now for and this is only for right now been used in triple negative breast cancer.
Although the recent studies to show that the addition of immunotherapy in selected patients with ER positive tumors also are have an additive effect.
But now with these advances in this shift that neoadjuvant therapy is preferred in almost all breast cancer patients except for maybe stage 1A and 1B. And that is a profound change in how we treat breast cancer And that APCR is associated with markedly improved outcomes.
And it gives us an insight within 6 to 8 weeks how well our patients
are going to do in contrast to our classic studies doing surgery 1st and then giving adjuvant therapy and then trying to measure 5 year survival rates 8 to 10 years later. So this is a very important advance. It allows us to keep moving on with new strategies and cancer management. The highest pathological response rates, around 63%, is used with the combination of pembrolizumab and a classic chemotherapy Carbotaxol followed by ACEC and the Pembro not only improves the PCR rates, but also results in smaller residual cancers across the entire spectrum of disease,
and that means it facilitates more conservative operations. It switches patients who needed a mastectomy for medical reasons into having the options of having lumpectomies because their tumors are smaller. So we also have learned that patients with residual disease have a poor prognosis and need additional or different treatment and allows us based upon the response to individualize their therapy. So this is our future, not only in breast cancer but in other tumors as well.
So this is another part of our advance which I’ll show you in other diseases as well. I showed you in Melanoma how we’re now eliminating the therapeutic no dissections in those patients who have APCR. This is from my colleague Henry Cure at MD Anderson who’s presenting this information for the first time next month in Miami and he kindly loaned me the slides to show to you today. So they have a prospective trial of eliminating breast surgery in selected patients who are exceptional responders for neoadjuvant systemic therapy. And the reason that they do this after their neoadjuvant therapy and
NOTE Confidence: 0.844040274545454
00:38:18.400 --> 00:38:21.310 they these are generally used with
NOTE Confidence: 0.844040274545454
00:38:21.310 --> 00:38:24.075 chemotherapy that they use a vacuum
NOTE Confidence: 0.844040274545454
00:38:24.075 --> 00:38:26.952 assisted core biopsy to in the area
NOTE Confidence: 0.844040274545454
00:38:26.952 --> 00:38:30.280 where the tumor is guided by ultrasound.
NOTE Confidence: 0.844040274545454
00:38:30.280 --> 00:38:32.578 And if there’s no residual disease
NOTE Confidence: 0.844040274545454
00:38:32.578 --> 00:38:35.160 they have no further breast surgery
NOTE Confidence: 0.844040274545454
00:38:35.160 --> 00:38:37.296 but if they have residual disease
NOTE Confidence: 0.844040274545454
00:38:37.296 --> 00:38:38.720 they get standard treatment.
NOTE Confidence: 0.844040274545454
00:38:38.720 --> 00:38:40.925 So Henry is presenting for the first
NOTE Confidence: 0.844040274545454
00:38:40.925 --> 00:38:43.079 time they’re multi institutional study,
NOTE Confidence: 0.844040274545454
00:38:43.080 --> 00:38:45.990 50 patients who had no breast
NOTE Confidence: 0.844040274545454
00:38:45.990 --> 00:38:48.365 surgery whose average size at the
NOTE Confidence: 0.844040274545454
00:38:48.365 --> 00:38:50.845 beginning was 2.3 centimeters and
NOTE Confidence: 0.844040274545454
00:38:50.845 --> 00:38:54.295 after a brief exposure to systemic
NOTE Confidence: 0.844040274545454
00:38:54.295 --> 00:38:57.276 chemotherapy was less than a centimeter.
NOTE Confidence: 0.844040274545454
They had to do 15 vacuum assisted biopsies in these patients. But here are the results so far, 62% had APCR among the triple negative breast cancer patients who had a checkpoint inhibitors plus chemotherapy was 71 percent, 55% in the her two positive. And what he’s going to present so far after 4.1 years of treatment with no surgical treatment, not a single patient has relapsed so far in the breast. And I could go over and show you other studies where we’re now looking at eliminating radiation therapy.
in these patients who have APCR. It’s changing how we treat patients based upon their responses to neoadjuvant treatment and they’re now doing a study not yet reported in patients getting systemic therapy standard lumpectomy and being randomized to getting no radiation therapy to the breast if they had APCR including in their lymph nodes. So let me as another example go over lung cancer. This is another example where the molecular profile profoundly effects our targeted treatment even in subsets.
of patients now of three to 7%. And in these small subsets we not only have first line therapy, second line therapy, even third line therapy for these small subsets defined by molecular markers. And as we do more of this, this is going to be the standard of care for all cancers as our molecular profile allows us to select patients who are responsive to certain systemic therapy, but not for others. But I wanted to show you in terms of the immunotherapy, how these first studies of using
neoadjuvant therapy had a major pathological response in 45% of patients. But the reason I wanted to show these slides is this is an example published in the New England Journal of Medicine of the pre treatment imaging. And after four weeks there was residual tumor. This was judged as a partial response, but when the surgeon took out that mass, there was no viable tumor left. And this is again illustrating and yet another disease, the importance of the surgeon doing the staging and giving
00:41:19.200 --> 00:41:21.080 the tumor to the pathologist.
NOTE Confidence: 0.90974770375

00:41:21.080 --> 00:41:23.355 Here’s another example from the same article,
NOTE Confidence: 0.90974770375

00:41:23.360 --> 00:41:25.880 fairly large tumor that didn’t move at all.
NOTE Confidence: 0.90974770375

00:41:25.880 --> 00:41:28.435 This was judged as a non response,
NOTE Confidence: 0.90974770375

00:41:28.440 --> 00:41:30.265 but nevertheless the surgeons took
NOTE Confidence: 0.90974770375

00:41:30.265 --> 00:41:32.946 it out and that mass that you’re
NOTE Confidence: 0.90974770375

00:41:32.946 --> 00:41:34.906 seeing on X-ray was replaced
NOTE Confidence: 0.90974770375

00:41:34.906 --> 00:41:37.280 completely by scar and inflammation,
NOTE Confidence: 0.90974770375

00:41:37.280 --> 00:41:38.618 it was APCR.
NOTE Confidence: 0.90974770375

00:41:38.618 --> 00:41:40.848 So now they’re randomized studies
NOTE Confidence: 0.90974770375

00:41:40.848 --> 00:41:42.400 of neoadjuvant therapy.
NOTE Confidence: 0.90974770375

00:41:42.400 --> 00:41:44.311 I’ll just go over this quickly in
NOTE Confidence: 0.90974770375

00:41:44.311 --> 00:41:46.476 the interest of time using either
NOTE Confidence: 0.90974770375

00:41:46.476 --> 00:41:47.760 nivolumab plus chemotherapy,
NOTE Confidence: 0.90974770375

00:41:47.760 --> 00:41:49.692 platinum doublets or pembrolizumib
NOTE Confidence: 0.90974770375

00:41:49.692 --> 00:41:52.107 with essentially the same results
in randomized studies. And you could see in this one study that adding the PD1 inhibitor nivolumab plus chemotherapy was better than chemotherapy alone. And in this study now moving from stage 3 to stage two lung cancer also demonstrated it with pembrolizumab that you get an additive effect with the hazard ratio of .58 in a highly significant difference in event free survival and later on follow up in overall survival. So these two studies are just two examples demonstrating the additive effect.
value of checkpoint inhibitors 

plus standard chemotherapy.

And the teaching point here is 

if you look at the responders in 

the outcome in the green lines, 

most of these patients will survive 

for a long time without relapsing. 

In fact, 

at MD Anderson and her Melanoma group, 

my colleagues tell me that it is 

less than 5% of patients who have 

APCR after neoadjuvant therapy have 

failed so far in their experience 

that now goes past five years. 

So let me show the last example 

on colorectal surgery,
which is also another area where neoadjuvant therapy here using chemotherapy and radiation therapy. And I don’t have time to go over the details other than to show you in randomized trials which I’ll just briefly show the results. Different combinations and sequences of chemotherapy and radiation therapy up front has caused a pathological or near pathological response in almost 50% of patients. So again just to show you the value of clinical trials in advancing our standards of care,
these are two randomized studies showing different combinations and sequences of radiation therapy, both short term and long term therapy and then whether the chemotherapy was given sequentially or simultaneously. But the bottom line is the patients who got longer exposures to standard chemotherapy as neoadjuvant therapy did, those did better than those who got shorter courses and this was shown in the repeater study. The this is a failure rate. Those patients who got longer courses of chemotherapy did better than those who had standard treatment.
And in this protege study now with seven years follow up that the patients who got radiation therapy first followed by long term course of more intensive chemotherapy with Fulfurinex did better than those who had the standard short term chemotherapy. And now overall survival at 7 years event free survival shows a benefit of this which became the standard treatment and in the experience at MD Anderson, this is from our Chair of Colorectal department, George Chang.
You could see those patients again that achieved APCR did better with long term follow up. These were 18% of the patients but no local recurrences in a very low risk of distant metastasis based upon the responses to the neoadjuvant therapy, again showing this in yet another disease as a strategy. And then finally this Oprah study which again randomized patients with different combinations of neoadjuvant chemotherapy, long term radiation therapy and chemotherapy and then we’re randomized to receive either watch and wait.
if clinically and by X-ray they had a clinical complete response. They went into a watch and wait program and the results of this we’re pretty striking. You can see that the patients who had the more intensive neoadjuvant therapy did better with long long course radiation therapy followed by FOLFOX. And the important point is that the that I wanted to show here is the three-year failure of the event free survival in patients who had no surgery was 53%.
then all of these patients were salvage with a TME operation.

But in those who had shorter courses of chemotherapy did not do as well.

But overall, nearly half the patients who received neoadjuvant therapy, especially with the longer courses of chemotherapy and longer courses of radiation therapy.

You can see that half of the patients avoided surgery even after six years of follow up. And those who recurred and had salvage surgery had essentially...
the same survival rates based upon the time of diagnosis as those patients who had surgery up front.

So I wanted to finish with what I think is an example of our future when we have the biomarkers that can give us an exact prediction of response rates with checkpoint inhibitors.

So in standard pathology report usually shows the immunochemistry results with either microsatellite instability high or mixed instability.

Responses in mismatch repair deficiency. Sorry. And the point here is this is
for the first time that the FDA approved a drug with checkpoint inhibitors based solely on the molecular profile. So regardless of which tumor type it is, colorectal, gastric, pediatric breasts, sarcomas which are very infrequent. The most common is in colorectal cancer which is 10 to 15% of patients have these biomarkers which is a surrogate for a poorly differentiated tumor. So think about it, the immune response is looking for foreigners, not self. The more foreign the object is in our body, the more robust the immune system is. So it shouldn’t surprise you that
00:48:41.130 --> 00:48:42.840 the more poorly differentiated tumor,
00:48:42.840 --> 00:48:45.720 higher tumor mutation burden or have
00:48:45.720 --> 00:48:49.125 these biomarkers are going to be the
00:48:49.125 --> 00:48:50.997 most responsive to immunotherapy.
00:48:51.000 --> 00:48:52.120 But this is dramatic.
00:48:52.120 --> 00:48:53.800 When the first studies were done,
00:48:53.800 --> 00:48:56.390 you can see there was a pathological
00:48:56.390 --> 00:48:59.085 major response in every patients
00:48:59.085 --> 00:49:02.329 who were treated with a checkpoint
00:49:02.329 --> 00:49:04.360 inhibitor and look at these results.
00:49:04.360 --> 00:49:07.587 A single dose of ipilumab and only
00:49:07.587 --> 00:49:11.220 two doses of nivolumab led to 100%
00:49:11.220 --> 00:49:13.540 pathological response in these
00:49:13.540 --> 00:49:16.845 patients who were MMR deficient and
00:49:16.845 --> 00:49:16.845
even in 27% of those who did not

have that mutation with this short
term dual agent and his larger series

have been presented like this.

At ASCO you could see that 95% of patients have expressing this biomarker in this case in colon cancer had a major pathological response at 67% had APCR with short term dual immunotherapy based upon this tumor marker. And here’s the other point is larger series have been reported again using one dose of IPI and at a low dose only 1 milligram per kilogram. Remember we started out at 10 milligrams, which was too toxic in that in 99% of
patients they had a pathological response.

So this is pretty dramatic.

Now for the surgeons.

This was published in the New England Journal of Medicine only on 12 patients who expressed this biomarker and who got a checkpoint inhibitor and based upon that response had no radiation therapy and no surgery and had been followed up now for more than four to five years.

And these aren’t small tumors. You could see in this example published in the New England Journal Medicine, these were large tumors that over
time with this checkpoint inhibitor

NOTE Confidence: 0.704941

disappeared and in these patients

NOTE Confidence: 0.704941

with the follow up with no radiation,

NOTE Confidence: 0.704941

no surgery,

NOTE Confidence: 0.704941

there were no recurrences based

NOTE Confidence: 0.704941

upon this tumor marker.

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So this also applies in the lower

NOTE Confidence: 0.704941

frequency of patients with GI tumors.

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Gastrointestinal and esophageal cancers,

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which you could see in these studies used

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in a combination of pembrolizumab and Folfox,

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achieved 23 of 26 patients were

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free of disease.

NOTE Confidence: 0.704941

And the overall survival in these patients

NOTE Confidence: 0.704941

who presented with advanced disease,

NOTE Confidence: 0.704941

treated with preoperative disease
and that 65% of those patients based upon the tumor marker, it’s a small percentage of patients had APCR with gastric and esophageal cancers. And now they’re going on in this series of trials, the first one in Cohort 1, they found APCR in 60% of patients with this MMR deficiency. The major response was 80%. And now the next phase of this trial is those patients who have a complete or near complete response radiologically and endoscopically get no surgery and follow up for GI.
for gastric and gastroesophageal malignancy.

So I’ve shown you in Melanoma, in lung cancer and breast cancer and now in colorectal cancer based upon tumor markers and usually based upon combinations of checkpoint inhibitors plus chemotherapy that we’re now moving in selected patients to not doing surgery and watch and wait and then follow up with the patients and in those that fail, which is still the minority of patients to do salvage surgery.

So these are my summary slides.

There are changes now, but these strategies I’ve told you.
are increasingly going to be applied for all solid tumors that will impact all of us in oncology fields. That new adjuvant therapies selected by tumor molecular profiles is now and will increasingly become the standard of care for most cancers, for all but the earliest stage 1 cancers. And that surgery is vitally important for staging and local regional Disease Control. I’ve showed you data that there may be a place for watch and wait, but that’s in a selected group of patients and then everybody else. There’s still an important role for.
surgery in staging these patients.

And interestingly now as we’re doing less surgery for early disease, we’re going to be doing more surgery for stage 4 and borderline resectable Stage 3 disease because we can downstage the patients.

And those of us treating even Stage 4 disease need to know whether the masses we’re seeing on X-ray is inflammation or viable tumor, take it out and do a molecular profile on those tumor cells that are not responding.

So we need to better refine the role of watch and wait. This is a new thing.
I’m not proposing it except in clinical trials and the intensity of follow up in the appropriate type of salvage surgery on relapse is going to be a new area for which we are going to need a lot of prospective data. And I think as I’ve shown you, we’re changing the standards of care based upon these prospective clinical trials that are neoadjuvant trials that involve surgery as part of the clinical trial. So surgeons must engage their patients in the clinical trials where appropriate and design surgical
trials to document the results. DE escalation strategies, new sequences of treatment and the results of salvage therapy. And I think for those training residents and fellows that surgical training must include more exposure to contemporary cancer management. And that the pool of American Board of Surgery certified surgical oncologist must increase to meet the demands in the public to have surgeons who are also trained in oncology to be part of the multidisciplinary team. And as many of you know at least in the tertiary hospitals that in
order to keep up with the rapidly moving field based upon one or two diseases are increasingly going to have to focus their treatment to one or two organ sites in order to stay current with the rapid advances. So here are my key messages for the surgeons: 1. Be prepared and informed to make major changes in the surgical management of your cancer practice, including deferring surgery until after a trial of neoadjuvant therapy. Because of the benefit I’ve shown you now in multiple tumor types, to consider surgical excision for
borderline or inoperable tumors that
are downstage with systemic therapy and
consider more conservative surgical
procedures with the downstaging.
And then we as surgeons have to adopt
A mindset of being an oncologist
who operates cancer management is
dealing with now a chronic disease.
Surgery is kind of a vertical specialty
that focuses on the operation
and the perioperative period.
But our job is not done once
the wounds have healed.
There is another phase for which
we need to be involved in giving
systemic therapy up front and how
we do what we do afterwards. And we also need to be at the arena when treatment plans are made to bring the surgeons perspective to multidisciplinary treatment. And without being critical, I know that your medical oncology training and radiation oncology training does not include surgery as part of your training and in fact you’re biased because you see our failures. I’ll give you one example. My daughter who’s APA in GI medical oncology at MD Anderson sees a few of these salvage surgery patients that
say our patients come in with these huge inoperable, miserable tumors. I don’t see why we’re doing salvage surgery. So I immediately called my son Glenn, who’s doing all the colorectal surgery and said, you know that happens but only in 5% of our patients. But my daughter thinks that we should be doing this because she sees the failures, the ones that do well don’t go to those medical oncology clinics. So I think it’s bringing the surgeon’s perspective to those that are different in medical and radiation oncology. And it’s the collective wisdom we
all bring that is better for patient
care decision making.
And then this last thing I
don’t have a solution for,
but I want to give you an example.
My son Glenn, who’s head of the
division of colorectal surgery at Emory
discussion with his chair.
So John Sweeney said Glenn,
I noticed your Rvus are down,
I noticed your Rvus are down,
what’s going on and Glenn responded.
Well, half of my rectal cancer
patients are getting a clinical
complete response and going into
watch and weight status and now I’m
00:58:17.335 --> 00:58:19.235 flooded with these patients doing flexible sigmoidoscopy exams every three months and there is little RVU values for this new group of patients. And so my point is in this new era of oncology management, how are we going to gain gauge the clinical performance that here to for is based upon volume of care. When oncology advances in all of our fields are driving us to perform less intensive therapy, surgeons are doing more conservative operation, less frequent lymphadenectomies, more watch and wait.
Radiation oncologists are going from six weeks standard courses to three weeks to weekly to no radiation oncology. So they’ll be less income if you’re doing shorter courses of radiation. And of course we’re a medical oncology colleagues. I think we’re going to be giving shorter courses of adjuvant therapy especially immunotherapy instead of one to two years of expensive drugs. And then what are we going to do with these patients who are in watch and are well patients that just need to be follow up.
the oncology specialist can’t see the new patients in those interactive treatment if they’re seeing well patients for follow up. So we have to delegate that follow up to mid level providers or even non oncology trained physicians who will follow these patients and send them back in those few that relapse and that’s a change in how we manage our patients. It’s a different team effect but with the like Glenn said if half of his patients are getting a clinical complete response, he can’t follow all of those.
00:59:53.088 --> 00:59:54.080 patients for a lifetime,

00:59:54.080 --> 00:59:56.520 somebody else has to do that and

00:59:56.520 --> 00:59:58.920 then send back those that relapse.

00:59:58.920 --> 01:00:01.678 So that’s the end of my talk.

01:00:01.680 --> 01:00:04.116 I hope that this has been helpful

01:00:04.116 --> 01:00:05.959 in telling you about our.

01:00:05.960 --> 01:00:07.670 Present and future strategies and

01:00:07.670 --> 01:00:10.228 how that will impact on the surgical

01:00:10.228 --> 01:00:12.624 management of our cancer patients and

01:00:12.624 --> 01:00:15.592 the value of clinical trials in make

01:00:15.592 --> 01:00:18.317 in changing our standards of care.

01:00:18.320 --> 01:00:20.328 So thank you all for the opportunity of

01:00:20.328 --> 01:00:22.436 coming and I hope this was helpful to you.

01:00:28.180 --> 01:00:30.825 Thank you for a talk that

01:00:30.825 --> 01:00:32.660 was uplifting, exciting
and also provocative.

I know that I was getting late.

There may be some time for one question from the audience for Hoocha.

So thank you, Charles, for presenting, really just giving us food for thought and talking about where cancer care is and perhaps where it's.

I want to come back to your last point, which is interdisciplinary collaborations.

And for the trainees in the room, I thought it'd be helpful to share a lens of, you know I was in Hopkins during that period and many of those first offers were felons.

Patrick Ford, the lung trial you showed and
was a fellow sitting in a conference and we were talking about this with surgeons, medical oncologists and radiation oncologists and the colorectal trials. My very good friend Louise Diaz and I remember sitting with Louise running our colon tumor board and an observation that was made on a small trial that on our phase one trial one of the patients was mismatched repair efficient, it was one patient and it was an observation made and wrote Suzanne Topallion, he’s a surgeon as you mentioned. He wrote that in the clinical Cancer Research it was an advance smaller.
01:01:44.805 --> 01:01:47.187 than this that led to this entire
NOTE Confidence: 0.832569248333333
01:01:47.187 --> 01:01:50.118 field of opening up in multiple tumor
NOTE Confidence: 0.832569248333333
01:01:50.118 --> 01:01:53.154 types from that very small observation.
NOTE Confidence: 0.832569248333333
01:01:53.160 --> 01:01:56.564 So my question to you is that how do
NOTE Confidence: 0.832569248333333
01:01:56.564 --> 01:01:58.790 we encourage that as we're becoming
NOTE Confidence: 0.832569248333333
01:01:58.864 --> 01:02:00.793 bigger that event happenstance that’s
NOTE Confidence: 0.832569248333333
01:02:00.793 --> 01:02:02.277 how research is done,
NOTE Confidence: 0.832569248333333
01:02:02.280 --> 01:02:05.727 that’s how great clinical initiatives happen.
NOTE Confidence: 0.832569248333333
01:02:05.727 --> 01:02:07.736 How do we foster that as leaders
NOTE Confidence: 0.832569248333333
01:02:07.736 --> 01:02:09.641 we’re sitting in this room that that’s
NOTE Confidence: 0.832569248333333
01:02:09.641 --> 01:02:11.255 a luxury that we barely have.
NOTE Confidence: 0.832569248333333
01:02:11.255 --> 01:02:13.600 So I wondered what’s your thoughts about,
NOTE Confidence: 0.832569248333333
01:02:13.600 --> 01:02:15.968 I think the answer is we’re if we’re
NOTE Confidence: 0.832569248333333
01:02:15.968 --> 01:02:17.960 looking for advances in care see
NOTE Confidence: 0.832569248333333
01:02:17.960 --> 01:02:21.348 opportunities and we can base a clinical
NOTE Confidence: 0.832569248333333
01:02:21.348 --> 01:02:23.800 trial prospectively on a hypothesis
or even retrospective data that leads to the design of the trial that we need to be thinking about.

We have to practice evidence based care. And if we don’t have this in this rapidly developing field, we’re going to go back to empirical medicine based upon marketing of drug companies and instrument companies.

So I think you know to add to what Nita has said that it’s so important for us to insist on our patients wherever possible being in clinical trials where they’re eligible so that we can advance the field based upon
evidence and not based upon marketing strategies but it. But we all need to have an open mind is you know and I’m enthusiastic about the results, but if you looked at the slides, there are a lot of patients who failed with our current treatment. So there’s still a lot to do and I think that’s going to be based upon the team working together, each bringing different perspectives. I love the story with Lei Ping Chen who said this works in the mouse, who said this works in the mouse, maybe it works in the patient and he brought that hypothesis to what
became a major immunotherapy advance.

So the collaboration and between the clinical teams and between the research teams and the clinical teams is I think the what’s important and championing the collective wisdom that we all bring with our different perspectives in bringing that together in our decision. Thank you very much. I think Doctor Balch will be here for a little bit longer. I don’t want to take more practice to this point. If you people can come down and
I know you'll be spending some time with the surgical residents, it's been wonderful. Thank you all for the honor of coming here today. No. And I get this. He get this luggage.