Substituting today very happy to be here.

So we have two talks today and I think it should be a very interesting hour.

Our first talk will be by Anne Chang and congratulations.

And so an is associate Professor of Medicine, medical oncology and Deputy Chief medical Officer and Chief Integration Officer.

As of about 3 hours ago.

She specializes in thoracic oncology with a background in translational research and metastases,
and a clinical focus has been built

has been to build an amazing small cell lung cancer program here with a comprehensive portfolio of clinical trials testing novel therapeutics.

Her research interests focus on focus and development of clinical trials and translational studies to test novel agents and combinations with immune checkpoint inhibitors for both small cell and non small cell lung tumors.

Over now nine years an she’s helped to build our smiling network,

which I think will hear about today and overseas operations quality
efforts in clinical research,
NOTE Confidence: 0.80177414
adult care centers.
NOTE Confidence: 0.80177414
She's a particular focus in quality
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measurement and improvement and
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his work to achieve ASCO copy
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certification for the entire smell.
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Academic clinical practice
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of actually received.
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Actually, the Joe Simone Award,
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just recently in Q just passed away
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last week, but a big honor for Masco,
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so an it’s a pleasure to have
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you here for our first talk.
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Transformation in quality building
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a cancer network,
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and.
Thanks Roy, it’s really a pleasure to be able to talk to you today and thanks for the invitation. I was trying to decide between lung cancer and the network, but because of the timing of the announcement this morning and I thought that it would be nice to highlight the work that has gone into building a cancer network. So that’s what I’m focusing, but I did put in a couple of slides with my trials so. I suck that in.

OK, so I’m sharing my screen my disclosures.
And this is for four.

If you recognize it, it’s South Ferry terminal farmers market in San Francisco and it’s amazing place because the quality of the food and the shops are really outstanding.

I had the best Peach I’ve ever had in my life.

The atmosphere is buzzing in the shops are full of colorful, beautiful produce as far as you can see and when I was here which seemed to me that this was more than a farmers market where each farmer sets up their shop.
individually next to each other, but somehow there was a transformation of the individual stands into a different collective entity, real community, and so in the same way that in the same way I want to talk about cancer or cancer network today, there really has been a trend over the past 10 years of academic institutions or other entities buying up practices or putting up their names on. Affiliated practices, but what I wanted to focus on is how I think we’ve built
a real transformative network, a community that is better than the individual units where cancer delivery is really somehow transformed. And so you know, this is, let’s go to transformation theory too as a guiding principle for this work. Carter said transformation is a process, not an event. And you start with a sense of urgency form a coalition and you create and share that vision. You empower others to act on that vision. You plan, create short term wins, consolidate those advances,
and hardwire new systems. And I think the bottom line.

Here is that quality improvement methodology is really been the basis of my job in the network and formed the foundation of building our vision over the past almost 10 years. So the objectives for today’s talk really are two number one provider, network development, overview, describe quality concepts and metrics and network development to discuss ways to further the research mission in the network. And then finally recognize the
benefits of expanded community.

So this is how it all began.

We started my job this was in 2011.

There was no network.

We hired anybody but we did have

Yale Smilow state of the art disease based,

patient centered clinical operation.

We had outstanding faculty,

staff,

trainees,

cutting edge clinical research

resources and across organizational

commitment for expansion and really

a powerful coalition of folks

to carry out that vision,

which was really to provide
comprehensive care to all patients. Close to home in Connecticut and to provide a platform for Yale Clinical Research and expand access to trials. So this is really the result. This is our clinical footprint in Connecticut and in Rhode Island. This stars are where our care centers are and we do provide care to patients within 30 minutes of where they live. In Connecticut. We provide care to about 45% of newly diagnosed cancer patients in Connecticut and we also provide about or.
We accrue about 25% of therapeutic clinical trial enrollments as, as Roy mentioned, we have achieved ASCO quality oncology certification throughout our entire network in the main campus. This is actually the only way to certify ambulatory practices. Many of you are familiar with the ACOS, which certifies cancer programs. In all of the physicians are what YM? With the exception of Hartford, where the physicians are still Saint Francis employed, but do have a faculty appointments and
are a stipend from Yale and all of the staff are Smilow employed or least, and we do have cross-system policies and procedures and quality initiatives. This is a timeline where I started here in 2011 and we did not have a network and then over the course of the next 9 1/2 years. We brought in a practices and We we brought in a practices and we brought in a practices and procedures and quality initiatives. In doing so really had the opportunity to have multiple PDF a cycles in terms of improving our process and improving our in perfecting our onboarding process and now as I said.
we have 15 locations in two states.

We have all we have almost 50 MD’s,

16 aips and over 400 staff we see

over 9000 new patients 100 and

over 25,000 treatment visits yearly and

the contribution margin on an annual

basis is greater than 110,000,000.

So I think that this is really been

successful and I’m going to talk a

little bit about the onboarding practice

the onboarding process first, so.

This is where we really utilized

integration and transformative change

strategies to engage the stakeholders.

The physicians that the staff

in the practice, and we.
There's at the bottom line is that there's really no shortcut here. It really is hard work having regular meetings on transition issues such as epic pharmacy, workflow changes, and those transitioned into practice meetings which were very useful. We developed a formal onboarding curriculum, and this utilized leaders and peers and the Smilow vision and structure. Faculty roles and expectations. What does it mean now to be part of
Yale and Smilow? How does quality work?

How does the research apparatus work?

Who are the dart leaders?

What is that mean?

What is what are academic mentors and and?

So going through that that curriculum also involving team building and leadership training and including our multidisciplinary members not only met Aachen Heme, but our surgical colleagues are rat out colleagues pain and palliative care so.

Um? Be the next.

Either or the next part of quality improvement is really measurement, and this is a graphic of the really PDS.
A cycle you have multiple.
You know, iterations of how do you improve care,
but measurement is really important,
and so we started measuring at baseline because we wanted to make sure that we could measure progress and not just, you know, stick a sign on the door.
That said, Yale Smilow and this paper published in 2018 really showed improvements in multiple domains of quality, including volume, clinical integration, quality metrics, and patient satisfaction.
I’m going to show you. Few of those.
At some of that data now.
So in annual visits for chemo this you can see the main campus in blue over the years and then. When the Kirsten’s Care Center started in in 2012, you could see the growth has really been significant and we do give now more chemo in our care centers closer to home for our patients than we do in the main campus. In terms of standardization, we utilized coping. Measurement Copy is a program through ASCO called quality Oncology Practice Initiative and it consists of.
NOTE Confidence: 0.8692515
00:10:45.110 --> 00:10:46.990 of ambulatory oncology,
NOTE Confidence: 0.8692515
00:10:46.990 --> 00:10:49.415 quality that have been developed
NOTE Confidence: 0.8692515
00:10:49.415 --> 00:10:51.355 national iyanar consensus based
NOTE Confidence: 0.8692515
00:10:51.355 --> 00:10:54.058 and evidence based when available,
NOTE Confidence: 0.8692515
00:10:54.060 --> 00:10:59.030 so we had a measurement at baseline.
NOTE Confidence: 0.8692515
00:10:59.030 --> 00:11:00.970 Representing the practices before they
NOTE Confidence: 0.8692515
00:11:00.970 --> 00:11:03.743 joined and then this is four years
NOTE Confidence: 0.8692515
00:11:03.743 --> 00:11:06.035 later we looked at the significant
NOTE Confidence: 0.8692515
00:11:06.035 --> 00:11:08.217 differences and saw that really the
NOTE Confidence: 0.8692515
00:11:08.217 --> 00:11:10.245 only changes were in the positive.
NOTE Confidence: 0.8692515
00:11:10.250 --> 00:11:12.847 These are actually shown here and and
NOTE Confidence: 0.8692515
00:11:12.847 --> 00:11:15.617 so this was really important to me
NOTE Confidence: 0.8692515
00:11:15.617 --> 00:11:18.400 because I wanted to make sure again
NOTE Confidence: 0.8692515
00:11:18.400 --> 00:11:22.114 it wasn’t just putting in a sign on the door,
NOTE Confidence: 0.8692515
00:11:22.114 --> 00:11:25.978 but that we were actually using.
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National consensus based metrics to show that we were improving quality for our patients. We also, as Roy mentioned at the beginning, did copy certification across our network and the academic campus. This is similar to the ACOs 26 standards and you really have to show in document that the process from soup to nuts of chemotherapy administration and policies and procedures are in place that show us. That are up to snuff for ASCO. Certification and we re certified in 2019.
Um, regarding clinical integration. I'll just show you the.

And this represents cases President care Center cases presented at smilow tumor boards. We have 13 disease specific multi tumor boards and we've asked all of our physicians to present one to two cases a month understanding that we can't present all of them. But really, those complex cases that need that multi D discussion needs to be presented and so you can see in 2013. This was difficult because the logistics around dialing in.
which is so easy now by assume it.

But at that time was very difficult.

Getting the path reviewed, getting the.

Radiology diagnostic imaging to be available that was really hard at the time and now I think we’ve received we’ve sort of the steady state, right around 500. That’s the case also.

Sorry, this is 2018-2019, 2020, right around the 500 mark, which I think represents sort of the steady state. Um, with respect to customer service. Those of you who have.
pay attention to press ganey know that we always cluster in this 90s area. It’s very difficult to make any changes here, but if you look at again baseline press ganey scores for practices that we acquired and six years later, you can see that in all of the cases we actually stayed the same. We're actually improved with one exception here is is this the site, but in some cases really significantly improved patient satisfaction. Um? This highlights some of the innovative projects that we've taken on in the network.
This was a pilot with Asko Asko. They have a quality training program that is 6 months and has three didactic sessions and a very aggressive curriculum every two weeks around process mapping and barrier analysis. In this case, we had a team from every care center at the time in 2000. In 2018, we did it again, and we had doctors partnering with nurses or nutrition, or in one case in MA Pharmacy, to conduct quality improvement projects. In all of those groups, we had doctors partnering with nurses or nutrition, or in one case in MA Pharmacy, to conduct quality improvement projects.
able to complete at least one PDS, a cycle over two years or each year, each year getting through. Apedia say cycle and this work ultimately resulted in nine story in five national presentations, one of those projects that Jane Kanowitz lead in water Ferd in 2018 is actually the care center quality goal for 2021. I think many of the participants in these projects were really energized by the teams and the learned around quality improvement.
And one question was how do we sustain that gain? You know, I think that it’s important to be able to use those tools in Q I2 to better care and recognize opportunities to reuse them to face challenges and. And this is actually what we’re doing now in the ambulatory transformation Work group we have. A number of groups that are really using the same Qi tools and change tools in lockstep. Action across multiple teams to respond to the pandemic and work towards transformation of care,
whether it’s relocation of sites or rapid uptake of Tele health.

Or you know, developing and disseminating best practices.

I think that this is the same process as the ASCO Smiler pilot but now applied to the immediate.

Now that we’re in, so you, I think you’ll hear more about these.

The work these groups are doing over the coming months, and I think it’s been really exciting.

So now I’m going to turn to clinical
research, and as I mentioned before, we have about 25% of our YCC therapeutic enrollments from the care centers. This is also a process that needed to be built and hardwired. This is back in 2012. We had three cooperative group trials open and we had to figure out how to do ESO. Peas, around drug shipment and lab processing and training the staff and the. The docs to do trials where they hadn’t done that before and as well as the Pisa trials to make sure that they were comfortable and had oversight of the process. Overtime we developed a monthly clinical...
research working group that has research champions from each site that meet monthly and vote on their portfolio.

The disease team leaders come to those meetings and present their portfolio and new trials, and I think that this process is really grown obviously here in the next slide you can see that the accrual per the yearly accrual by sight and the highest sites. Saint Francis Northaven Trumbull, Fairfield. I think one of the things we’ve learned is that they need to have or they have a ACRSL lab which allows all protocols.
No, let’s which.

Means that there’s no limit on protocols that they can open due to lab processing times.

Certainly the 2020 accrual was affected by Covid Inc.

In our in 2018 we had 224 this year.

If you take out the months that we had covid and we had very good accrual prior and have really picked up now we would have certainly hit 200 between 200 and 220.

If not for the for covid, so we activated a new site this year in Westerly.

They are now treating some of the patients who were started in Waterford and.
Now, in Rhode Island and you can see it actually in Waterford, which opened three years ago. There's been really great accrual growth there as well, so I think that there's really a lot of potential here if the next slide shows you the yearly accrual by the DART.

So which kinds of trials are having the best accrual breast in GI have are certainly at the top. The long and heme are not far behind as well as T rad ngu that are increasing,
so I think again, there’s a tremendous potential here in the care centers, and as we have all. Our docs aligning with disease teams. I think this will just increase in the future. Um, this is the. I will quote Kurt Sabbath, who is one of our care center docs who helped to lead research initially. Kurt always said that he felt that clinical research is synonymous with quality care because there’s so many eyes on the patient. There’s so much emphasis on important communication,
shared decision making, and that really epitomizes quality. In our case, the vision had always been to provide research as access to our patients close at home, and I think that even more than the numbers per site, this is what really strikes me. Every year we have somewhere around 85% to 87% of our physicians who put at least one patient onto trial. So I think we really changed that culture. We’ve had a research summit every year, usually around 80 people.
That includes our care center docs or DART team members or CTO staff get prizes.

We have about 13 care center physicians who served as PII on trials and right now we have 83 trials open in nine disease types.

Approximately 50% cooperative group, 43% industry sponsored in 10% IIT’s.

Our care center accruals form about 60% of our cooperative group trials, so that’s really important.

This is one of my trials. This is a national trial that we have opened in about 900 sites across the US and Canada.
but in our care centers as well.

I’m National Co chair with has poor guy and it’s a first line PDL

positive trial for non squamous non small cell and I think that this is an important trial because it either randomizes you two arms which start with immunotherapy and then if you progress you going to chemo. Or you add chemo to the pen bro Appan progression. That’s an important question. This is the the chemo IO control arm and this trial I think will tell us. Very important.
Give us information on sequencing of chemo.

If you can spare it upfront.

If you add it to the immunotherapy if that will help.

And ultimately because we are collecting tissue from this trial,

we're going to be looking for prognostic signatures for Pember Lizum app and predictive signatures for addition of chemo to immunotherapy. This is also an IIT of mine in small cell which with the biopsy upfront and then on treatment at week four after after treatment with EPI,

Nevo and this trial has 17 patients who started on it with 10 paired pre
and on treatment biopsies and this trial is open in our network and we’ve had 11 accruals from our network and I think that’s important because. Talking to colleagues of bars across the country who have networks and who are trying to do. Clinical trials they’ve really relied on industry sponsored the cooperative, and very few actually have have diploid Ilits in in the network. So this this just shows you a number of the items that we have and you can see that here’s 12 accruals or 30% of Doctor Lacey’s modified folfirinox,
and in this case Doctor Kim Johans.

That’s 88% of her seven out of eight accruals for her and you know, for Doctor Nipper, it’s a 4040% of her accruals for her IIT as well so. I think this is really important research and support of our investigators at Yale.

So what is the future hold? Among other things, I think there are certainly opportunities for building multidisciplinary care to enhance our Smiler signature of care in the network and to build on our current Med. Onken Hemang Craddock networks to
support and our surgical oncology
representation.
We are developing formalized multi
clinics and that some of the work
integration role and strengthen
our alignment with disease teams.
And certainly our disease centers
provide service excellence
and positive patient outcomes.
This is my favorite slide.
And certainly our disease centers
provide service excellence
and positive patient outcomes.
This is my favorite slide.
This is what I think is the most
exciting piece of all of this
is not numbers of patients,
better faculty that have
00:25:10.854 --> 00:25:13.910 joined his care center is one of them.
NOTE Confidence: 0.8432984
00:25:13.910 --> 00:25:16.328 Francesca is going to give a
NOTE Confidence: 0.8432984
00:25:16.328 --> 00:25:18.250 grand rounds right after me.
NOTE Confidence: 0.8432984
00:25:18.250 --> 00:25:20.218 They all master clinicians.
NOTE Confidence: 0.8432984
00:25:20.218 --> 00:25:23.170 They have devoted their really the
NOTE Confidence: 0.8432984
00:25:23.254 --> 00:25:26.173 clinical arm of a female cancer and
NOTE Confidence: 0.8432984
00:25:26.173 --> 00:25:28.426 smilow cancer hospital within the
NOTE Confidence: 0.8432984
00:25:28.426 --> 00:25:31.180 within the community and all have
NOTE Confidence: 0.8432984
00:25:31.261 --> 00:25:33.463 joined with the disease teams to
NOTE Confidence: 0.8432984
00:25:33.463 --> 00:25:36.528 do you know any number of really
NOTE Confidence: 0.8432984
00:25:36.528 --> 00:25:37.538 exciting things.
NOTE Confidence: 0.8432984
00:25:37.540 --> 00:25:39.730 BPI on trials do collaborative
NOTE Confidence: 0.8432984
00:25:39.730 --> 00:25:42.110 research projects, develop Qi projects,
NOTE Confidence: 0.8432984
00:25:42.110 --> 00:25:45.110 help teaching our house staff and
NOTE Confidence: 0.8432984
00:25:45.110 --> 00:25:48.065 anymore so it has really been my
NOTE Confidence: 0.8432984
00:25:48.065 --> 00:25:50.482 honor to represent these folks and
to work with them. And I can’t.
I can’t emphasize enough that it’s
really been a work collaborative
work of many, many,
many hands to build the network,
including Charlie and Lori.
Kevin Billingsley,
Kim’s lesser art film, Aleesa Chomsky,
Monica Fradkin, Connie Engelking,
Roy Herbst,
Stephanie Pauline, have invested so forth.
Jeremy Court Manske will take over as the
Chief Network Officer for Medical Services
and head up the medication he Monk.
And I will be focused on really developing
the service lines and integration
with our delivery care networks.

So thank you for the time and.

Think I’m done so I’d love to
answer any questions if if there
were any. Thanks and that was wonderful.

And congratulations on a very well
deserved promotion and we see why.

So we have a few questions.

Please put them in the chat.

Melinda Erling comments were lucky to have
this infrastructure with the care centers.

I know a lot of non therapeutic
interventional research being done in the
care centers related to tobacco control,
nutrition, exercise and obesity,
00:27:03.112 --> 00:27:06.748 so I will just follow up and say no.

00:27:06.750 --> 00:27:07.533 Make it secure.

00:27:07.533 --> 00:27:09.099 Diverse state as you go up

00:27:09.099 --> 00:27:10.610 and down the 95 corridor.

00:27:10.610 --> 00:27:12.546 How are we trying to help increase the
diversity of our patient population at

00:27:12.546 --> 00:27:14.107 our care centers to get more patients

00:27:14.107 --> 00:27:16.046 from diverse backgrounds on trials?

00:27:16.046 --> 00:27:17.786 That’s certainly something that

00:27:17.790 --> 00:27:18.822 we can now do that we have so

00:27:18.822 --> 00:27:21.014 much integration within the state.

00:27:21.014 --> 00:27:22.479 Great great question.

00:27:24.830 --> 00:27:26.226 I’m just going to go back and share

00:27:26.226 --> 00:27:28.997 my screen again so you can see

00:27:28.997 --> 00:27:31.118 who’s doing a lot of this work.

00:27:31.118 --> 00:27:33.135 NOTE Confidence: 0.905967
You know, Melinda, that’s a planted question because we just put together a narrow one to study the lean interventions in the care centers, and I think that’s going to be really exciting groups if you look here. This is Andrea Silver and she’s done a lot of work actually devoted, you know, one of her passions is in increasing under increasing representation of of. And she’s done a number of things, including that grant the initial grant called own it.
which was oncology works
with New Haven getting.
Community representatives to
weigh in on what kind of research
is done in the in at smilow and
building those relationships.
I think that you know our our latest
cancer Grant has been incredibly.
You know there's been a big focus on
trying to increase representation of of
of folks in our in our clinical trials,
and that certainly is a focus for us.
Right, that’s that wonderful one.
More question.
And then we’ll move on.
Someone comments. It’s amazing how you built these tumor boards, even before anyone knew what zoom was. So now that we have zoom in, everyone can zoom from their phone from their walk. Can we use this technology to further integrate? You know multi modality, care subspecialty care with you. showed us 55 or so doctors around the state. Are we using these tools of Tele Health to do even better now to integrate our care? Yeah, I mean, I think that with covid we’ve really we toggled up
to over 50% of usage and adoption of telehealth during last spring. And I think that we have.

You know initiatives on next day access and improving access that we can utilize Tele health for, and certainly within our multi D clinics were thinking about doing that as well. I think there’s a lot of innovation and non therapeutics, but we certainly have used the care centers as places to participate with the smoking cessation.
Joe Biden Moon shot initiative.

As well as.

You know collect samples for Stephanie, Aliens, NDS, registry and attempts to understand the science behind that.

So I think there’s just you know no end to what you can do with the resources and the team that we have.

Great well thanks Anne. Wonderful talking again,

congratulations.

So we have a second speaker,

it’s Doctor Francisca Montinari.

Doctor Martner.

Doctor Martin Ari is an assistant.
professor of clinical medicine in the hematology section and cares for patients with hematologic malignancies at our southernmost care center in Greenwich. 

Documentary recently joined Yell from the New York Presbyterian Hospital, Columbia University Medical Center, College of Physicians and Surgeons, which she was assistant Professor of medicine and Experimental Therapies Therapeutics in the Center for Lymphoid Malignancies.

Doctor Montanari received her medical degree from the University of Pavia in Italy, from which she graduated Magna ***
laude and completed both residency and Fellowship and New York University School of Medicine, but she was awarded the Fellow of the Year Teaching Award. She served on the Institutional Review Board Committee and as director of the Institutional Lymphoma Tumor Board at Columbia University, and he is part of the steering committee of the Lymphoma Research Foundation, Lymphoma rounds were so lucky to have been able to recruit Francisca recently, and she’s going to talk to us now. About post transplant.
00:31:23.364 --> 00:31:25.488 lymphoproliferative disorders franceska.

00:31:27.850 --> 00:31:30.310 Thank you for the introduction, so I'll share my screen.

00:31:37.680 --> 00:31:40.707 OK, so good afternoon everybody.

00:31:40.707 --> 00:31:44.421 I will review today was transparently proliferative disorders.

00:31:44.421 --> 00:31:45.930 So here's my disclosures. So we are.

00:31:45.930 --> 00:31:49.759 We will review together and how PLD are classified according to the most recent WHL classification,

00:31:49.760 --> 00:31:53.491 the Epidemiology, the risk factors at timing of onset prognosis,

00:31:53.491 --> 00:31:56.308 and therapeutic options including a current treatment paradigms, ongoing clinical trials and

00:31:56.308 --> 00:31:58.560 ongoing clinical trials and

NOTE Confidence: 0.7702043
future directions.

So let’s start with the classification under the revised 2016 W 2 classification post. Transplant lymphoproliferative disorder are classified under the immune deficiency. Associated lymphoproliferative disorders, along with lymphoproliferative diseases associated with primary immune disorder, HIV infection and other iatrogenic immunodeficiency. Um, by definition they are any lymphoid or plasmacytic proliferation that develop as a consequence of immuno suppression. In order sequence of a solid organ or stem cell allograft, it is considered officiality.
And based on the new classification, the device classification detailed include nondestructive PTL. These further subclassified into plasmacytic hyperplasia. Infectious modern closes like and Florida follicular pleasure which is a new entity under the new revision, polymorphic deity monomorphic TLD that comes into the B cell neoplasm and classical Hodgkin lymphoma. So purely nondestructive, these diseases are classified based on the pathology major.
findings and undersell prevalence.

There is usually preservation of the architecture, and these are polyclonal B cell proliferation by immunophenotyping genetic studies.

There typically be positive the responsive to MENA suppression reduction in most of the cases and they are usually seen in kids. So in the pediatric population. So we do see on the bottom an example of plasmacytic hyperplasia with the preservation of the architecture of the lymph node and infiltrates of abundant plasma cells. Peter D.
Polymorphic this is an entity that is characterized by either a genius mix of immunoblastic plasma cell and different size. The lymphocytes. The architectural is the architecture is usually faced. These are mostly polyclonal but presence of monoclonal B cell have been described and detected by immuno phenotype and genetic tool. There mostly EBV positive and some of them have been sealed. Six somatic hypermutation. So here’s an example of architectural effacement on the left.
00:34:38.530 --> 00:34:41.057 with the associated to a large area
NOTE Confidence: 0.7702043
00:34:41.057 --> 00:34:44.014 of necrosis and on the right variable
NOTE Confidence: 0.7702043
00:34:44.014 --> 00:34:46.259 size and shape lymphoid infiltrate.
NOTE Confidence: 0.80955
00:34:48.510 --> 00:34:50.784 Monomorphic PTSD, those are the one
NOTE Confidence: 0.80955
00:34:50.784 --> 00:34:53.708 that do fulfill the criteria for non
NOTE Confidence: 0.80955
00:34:53.708 --> 00:34:56.372 Hodgkin lymphoma or plasma cell neoplasm,
NOTE Confidence: 0.80955
00:34:56.380 --> 00:34:59.082 small B cell lymphoma are not considered
NOTE Confidence: 0.80955
00:34:59.082 --> 00:35:01.760 at not the designated as PTLT,
NOTE Confidence: 0.80955
00:35:01.760 --> 00:35:04.686 with the exception of the beaded positive
NOTE Confidence: 0.80955
00:35:04.686 --> 00:35:06.854 extranodal marginal zone lymphoma that
NOTE Confidence: 0.80955
00:35:06.854 --> 00:35:09.398 usually arise in the cutaneous or
NOTE Confidence: 0.80955
00:35:09.398 --> 00:35:11.859 subcutaneous tissue and this is because
NOTE Confidence: 0.80955
00:35:11.859 --> 00:35:13.403 their standardized incidence ratio
NOTE Confidence: 0.80955
00:35:13.403 --> 00:35:16.325 is not different than in the regular
NOTE Confidence: 0.80955
00:35:16.325 --> 00:35:19.209 population and they’re not started to happen.
NOTE Confidence: 0.80955
00:35:19.210 --> 00:35:21.765 As a consequence of the immune suppression,
Besides those any other kind of non-Hodgkin lymphoma is considered uppity ality. So the architecture defacement is usually present. Immuno, phenotypic and genetic features are typically recapitulating what we do see individual competent counterpart. And here I included an example on the left of. You should be selling for infiltrating. Lymph node and underwrite dereza. An example. This is a renal allograft biopsy with the showing about this planning T cell gamma,
T cell lymphoma with the characteristic infiltration of the small blood vessels. Finally, classical Hodgkin lymphoma has also been associated and described in the setting of post transplant and is considered to be APTLD. It fulfills the criteria for the high school informing that we do see and immunocompetent population, but is typically mixed cellularity. It’s always EBV positive and we do see that predominantly in the renal transplant recipients. Therapies treated like the Hodgkin lymphoma and immunocompetent counterpart.
and here an example of a release time. Excel on the bottom surrounded by an inflammatory background of lymphocytes and using fields. And this is our typical greatest number Excel with the city 20 CD 30 positive ITI. So very very Inter genius group of diseases. And so how? How frequently are our diesel informers? So we do about 40,000 transplant every year in the United States and period is the second most common malignancy in this patient population behind non Melanoma skin cancer. So it accounts for 21% of all the
cancers in recipients of solid organ transplant as compared to only four to 5% of the cancers and immuno competent population. The incidence has increased over the past two decades and this is for a variety of reasons. The increased age at the older age of the Gilded Age of and owner and recipients new immunosuppressive treatment. The introduction of the haploidentical stem cell transplant and improved awareness of the disease and diagnostic schools. So after a solid organ transplant, the risk of developing a PLD varies for over 20% two point,
8% depending on the organ transplanted

multi visceral intestinal being associated

followed by lung,

heart,

liver,

pancreas and with kidney being

the carrying the lower risk for

The risks varies based on the

HLA degree of the HLA matching.

And the and the need for T cell depletion. So it is a highest for upload denticle

without this addition 20% and it goes down to 3% in recipients of matched

related dollar hematopoetic stem
cell transplant. So what do we know in terms of risk factors besides the type of the transplant of the transplanted organ or the type of allogeneic stem cell transplant?

For recipients of solid organ transplant, it is an established risk factor.

The degree of Mr. EBV mismatch at the time of transplantation with the recipients being a big negative and the donor EBV positive.

Also, the intensity of the induction, immunosuppression, treatment and duration of maintenance therapy, including increased the need of
treatment due to graft rejection episodes.

There is a strong evidence associated with the use of certain immunosuppressive drug.

And in contact with others that are less associated and weak, evidence of risk is associated with infectious diseases and non EBV infection for instance, and other characteristics, genetic characteristics or underlying comorbidities of the host. For hematopoietic stem cell transplant recipient, age seems to be the biggest risk.
factor for development of these
diseases and the conditioning.

Regiment. Um also, um.

So in terms of timing,
typically PTSD arrives early in
the setting of hematopoetic stem.
The transplant and leader in the
setting of a solid organ transplant,
but it’s not really that predictable.
We considered an early onset if the
PTSD arise in the first year after
the transplant and the late onset,
if it arises a year later.
Starting one year after the transplant and.
And the reason the battle,
the pathogenesis is associated in the
early onset to an acute EBV infection or a reactivation of the virus in the setting of a reduction of the MTV cytotoxic T cell lymphocytes, usually early PTLDREB positive, and frequently there is the allograft is involved. In the late onset there have been many hypothesis so hidden around the infection with the baby, then resolved and lymphoma keeps developing other viruses besides BV has been hypothesized as playing a role such as CMV, a persistent antigenic stimulation.
done by the allograft and lymphocyte deregulation in the setting of a chronic immuno suppressed state. These are usually. More likely,
extra node with Extranodal involvement, not necessarily involving the graft and the monomorphic subtype is the most common. So what do we know about the prognosis of this disease that are regarding prognosis are mostly from single institution retrospective analysis and during my time at Columbia University I work on setting up a tumor bank for this disease with pathological.
00:41:42.773 --> 00:41:45.278 specimen link to clinical information,

00:41:45.280 --> 00:41:47.905 and this is what we have learned

00:41:47.905 --> 00:41:50.309 from the analysis of 120 patients.

00:41:50.310 --> 00:41:52.368 This is the largest series published

00:41:52.368 --> 00:41:54.949 so far on this specific disease.

00:41:54.950 --> 00:41:55.374 Interestingly,

00:41:55.374 --> 00:41:57.070 most of the clinical.

00:41:57.070 --> 00:41:59.180 Features that we think might

00:41:59.180 --> 00:42:01.784 predict an outcome might have an

00:42:01.784 --> 00:42:03.849 impact on the overall survival.

00:42:03.850 --> 00:42:05.970 Did not correlate with overall

00:42:05.970 --> 00:42:08.090 survival in our patient population,

00:42:08.090 --> 00:42:10.640 including the subtype of the PTSD,

00:42:10.640 --> 00:42:13.510 the decade of diagnosis prior or after

00:42:13.510 --> 00:42:15.729 the introduction of their attack.
Some organ do kind of organ transplanted
NOTE Confidence: 0.8300465
DV status, graft involvement,
NOTE Confidence: 0.8300465
and extranodal involvement
NOTE Confidence: 0.8300465
or stage of diagnosis.
NOTE Confidence: 0.8300465
So using a recursive partitioning model,
NOTE Confidence: 0.8300465
we separated patient.
NOTE Confidence: 0.8300465
Recursively,
NOTE Confidence: 0.8300465
at each step into two distinct
NOTE Confidence: 0.8300465
groups based on the variables that
NOTE Confidence: 0.8300465
provided the maximal separation based
NOTE Confidence: 0.8300465
on survival and using this model,
NOTE Confidence: 0.8300465
we were able to identify based on
NOTE Confidence: 0.8300465
age CD 20 expression and equal status
NOTE Confidence: 0.8300465
for groups that were well separated
NOTE Confidence: 0.8300465
in terms of roll survival and with
NOTE Confidence: 0.8300465
an even number of patient and in the
The lowest group we can see that the medium overall survival was not reached. Those were essentially mostly pediatric patients with a good performance status. What is in the very high risk group elderly with a foot Burma status and essentially all patients with the CD negative disease. The median overall survival was as short as one point 3 months. So what else we have learned, we know very well that T cell lymphoma have a much worse prognosis than Bissell informal immunocompetent population. But what are?
What is the behavior of this LPT?

LD is not well, no, not due to the rarity of these diseases.

So we did analyze in our series of pulling over monomorphic PTSD and the differences between B cells and T cell TLD.

And we do see that they sort of recapitulate what we do see and immuno competent counterpart in terms of prognosis with the median overall survival being very low for the T cell and compared to the diesel in monomorphic PLD.

Also, we did observe that the time of the median time to answer it was much longer for T cell nine years.
00:44:02.421 --> 00:44:04.899 compared to three years for the B cell type and all T cell period in our series were leaving negative.

00:44:10.690 --> 00:44:13.539 Another thing that we have also learned is that importance of more marrow of staging and the incidents of more involvement in the PLD.

00:44:22.520 --> 00:44:26.056 It is very common in our series of patients at 23% of monomorphic PLD.

00:44:26.056 --> 00:44:28.920 patients at 23% of monomorphic PLD.

00:44:28.920 --> 00:44:31.570 had bone marrow involvement compared to the in T cell subtypes.

00:44:31.570 --> 00:44:35.030 in the T cell subtypes.

00:44:35.030 --> 00:44:35.514 Also, polymorphic exhibited our very high bone marrow involvement.

00:44:35.514 --> 00:44:37.450 high bone marrow involvement.

00:44:37.450 --> 00:44:39.386 high bone marrow involvement.

00:44:39.390 --> 00:44:42.393 All the cases of polymorphic with
where bone marrow involvement was detected.
This resulted in up stage of the disease.
And ever involvement was associated with poorer outcome.

So we did compare the incidence of the involvement of Lombardy Boomer involvement in monomorphic PTSD compared to the normal diffuse large B cell.
lymphoma and HIV diffuse large B cell lymphoma patients diagnosed during the same time frame at our institution.
and we do see here that monomorphic, detailed involvement compared to the HIV positive diffuse large B cell involvement and this is suggest that immuno compromised.
State regardless of videology

vial associated or higher trajanic

maybe is a major risk factor for dissemination to the marrow.

Finally,

this is a loser.

Analyze last year actually two years ago and this was presented at ASH in 2019.

We did analyze the data regarding the cell of origin and the impact of treatment on the outcome of diffuse large B cell lymphoma.

So these type and in our series non germinal center was more common than germinal center.
I just want to highlight here that as previously reported and non germinal center PTSD is usually be positive versus germinal center is usually it will be negative clinical characteristic, organ transplant, immunosuppressive, treatment time of onset was not different in these two subtypes and there is a trend suggesting a better outcome, a better PFS and OS in patients with. Germinal standard compared to non germinal center mirroring the outcome in Indiana competent population and RE broker did not improve overall survival or progression.
Free survival were compared to R chop but in not resulted also either in an increase.

Toxicity in our series was extremely low and only one patient died in each treatment group.

So the current challenges for PT LDR therapy are uncommon disease, as we saw there is a big originality in the type of PTSD that is it originality in the patient population, and immunosuppressive treatment they receive that is a high mortality rate.
that is associated with the chemotherapy and this is usually in length to the increased risk of infection that we do see in these patients. Population and unique to this patient population is the risk of graft failure. So currently general principle of treatment include immunosuppression reduction. I just want to mention that the only perspective trial that utilize immuno suppression reduction as part of a sequential treatment for this disease on a very large sample of you know on a very large number of patients 160 patient showed a 40% incidence of acute graft reaction.
So typical in the adult population.

Immunosuppression reduction is utilized at the same time.

Other interventions such as rituximab are or combination.

Chemotherapy surgery, radiation therapy. Unlikely.

What we do see in Hodgkin and an article in former is a well established the treatment for stage one disease, PTSD and in the relapsed and refractory setting.

There are adoptive immunotherapy utilizing EBV specific cytotoxic T cells and high dose chemotherapy.
00:48:21.653 --> 00:48:24.845 with a toddler stem cell transplant
NOTE Confidence: 0.7767812
00:48:24.935 --> 00:48:26.907 or both being explored.
NOTE Confidence: 0.7767812
00:48:26.910 --> 00:48:30.886 So there are only few prospective trials,
NOTE Confidence: 0.7767812
00:48:30.890 --> 00:48:33.170 primarily on polymorphic and
NOTE Confidence: 0.7767812
00:48:33.170 --> 00:48:36.622 monomorphic beissel. PTSD and hold the.
NOTE Confidence: 0.7767812
00:48:36.622 --> 00:48:38.934 Stop for trials here.
NOTE Confidence: 0.7767812
00:48:38.940 --> 00:48:39.310 Um,
NOTE Confidence: 0.7767812
00:48:39.310 --> 00:48:41.900 use their attack some as a single
NOTE Confidence: 0.7767812
00:48:41.900 --> 00:48:45.082 agent with a very high with a good
NOTE Confidence: 0.7767812
00:48:45.082 --> 00:48:47.589 overall response rate under an CR rate,
NOTE Confidence: 0.7767812
00:48:47.590 --> 00:48:49.290 but not exciting overall survival
NOTE Confidence: 0.7767812
00:48:49.290 --> 00:48:51.792 due to early relapse is the best
NOTE Confidence: 0.7767812
00:48:51.792 --> 00:48:53.642 results that have been achieved
NOTE Confidence: 0.7767812
00:48:53.642 --> 00:48:55.622 that utilizing either a sequential
NOTE Confidence: 0.7767812
00:48:55.622 --> 00:48:57.647 treatment or a risk stratifies
NOTE Confidence: 0.7767812
00:48:57.647 --> 00:48:59.830 sequential treatment and this is the
NOTE Confidence: 0.7767812
00:48:59.830 --> 00:49:02.070 PTL D1 trials that is the largest
NOTE Confidence: 0.7767812
00:49:02.143 --> 00:49:04.313 phase two trial ever conducted
NOTE Confidence: 0.7767812
00:49:04.313 --> 00:49:06.483 in this patient population and
NOTE Confidence: 0.7767812
00:49:06.554 --> 00:49:08.190 reported by the German.
NOTE Confidence: 0.7767812
00:49:08.190 --> 00:49:10.810 Study group so will review
NOTE Confidence: 0.7767812
00:49:10.810 --> 00:49:14.090 the results of the PD L D1.
NOTE Confidence: 0.7767812
NOTE Confidence: 0.7767812
00:49:16.550 --> 00:49:21.485 This was published in JCO in 2017.
NOTE Confidence: 0.7767812
00:49:21.490 --> 00:49:23.608 Patients were with that newly diagnosis
NOTE Confidence: 0.7767812
00:49:23.608 --> 00:49:28.281 of PTSD received an induction treatment
NOTE Confidence: 0.7767812
00:49:25.881 --> 00:49:28.281 with rituximab and then based on
NOTE Confidence: 0.7767812
00:49:28.281 --> 00:49:31.873 their response they received the
NOTE Confidence: 0.7767812
00:49:30.317 --> 00:49:31.873 consolidation with rituximab alone
NOTE Confidence: 0.7767812
00:49:31.873 --> 00:49:34.580 or they were escalated to our CHOP
NOTE Confidence: 0.7767812
00:49:34.580 --> 00:49:36.890 and 152 patients were enrolled again.
NOTE Confidence: 0.7767812
This is the largest study in this disease that has ever been conducted and we do still at 1/4 of them after the initial induction with maximum achieved a CR and these were the patient that did not receive. Instead of toxic treatment, the overall response rate was a diet CR rate 70%.

Army generation of response was not reached and let me down. Overall survival was 6.6 years. Treatment related mortality in this study was 8% which is the lowest reported in this patient population and
00:50:12.820 --> 00:50:14.080 this is a attribute.

00:50:14.080 --> 00:50:16.114 This has been attributed to the

00:50:16.114 --> 00:50:18.998 fact that a quarter of the patients

00:50:18.998 --> 00:50:20.938 were spared cytotoxic chemotherapy.

00:50:20.940 --> 00:50:24.210 So. What’s new in PID.

00:50:24.210 --> 00:50:26.245 Recently over the past five

00:50:26.245 --> 00:50:29.196 years it has been more and more

00:50:29.196 --> 00:50:31.698 recognized than PTSD tend to be.

00:50:31.700 --> 00:50:35.860 CD 30 positive So this is a study by vision.

00:50:35.860 --> 00:50:38.164 Others that showed that out of

00:50:38.164 --> 00:50:40.242 108 patients with PTSD diagnosed

00:50:40.242 --> 00:50:43.375 between 1994 and 2011, it was 85%.

00:50:43.375 --> 00:50:46.350 Of this patient expresses CD 30 including

00:50:46.439 --> 00:50:49.585 81% of the diffuse large B cell lymphoma.

00:50:49.590 --> 00:50:52.030 This is very particular to

00:50:52.030 --> 00:50:54.045 the other side.
the query after the PTLD.

Because in the immunocompetent,

00:50:55.990 --> 00:50:58.270 if you started selling for my

usually city third expression is

probably less than 20% and not only

demonstrated a high CD 30 expression.

They also demonstrated that it was

associated with a better outcome. So.

Twice this interesting or important,

we now have a drug that targets

specifically city 30 brentuximab windowed

and is an antibody drug conjugate

that binds to the city 30 and one.

Since the internalised release,

monumental restarting E which is

microtubule disrupting agent which
NOTE Confidence: 0.82772666
00:51:31.573 --> 00:51:33.643 end up like causing apoptosis.
NOTE Confidence: 0.82772666
00:51:33.650 --> 00:51:35.034 As we all know,
NOTE Confidence: 0.82772666
00:51:35.034 --> 00:51:37.110 grant access method Odin is now
NOTE Confidence: 0.82772666
00:51:37.193 --> 00:51:40.063 approved with various indication in
NOTE Confidence: 0.82772666
00:51:40.063 --> 00:51:42.359 Hodgkin lymphoma anaplastic large.
NOTE Confidence: 0.82772666
00:51:42.360 --> 00:51:44.940 Calling from.
NOTE Confidence: 0.82772666
00:51:44.940 --> 00:51:46.293 So in 2019,
NOTE Confidence: 0.82772666
00:51:46.293 --> 00:51:48.097 at the ASH meeting,
NOTE Confidence: 0.82772666
00:51:48.100 --> 00:51:50.760 the results of these Phase 1 two
NOTE Confidence: 0.82772666
00:51:50.760 --> 00:51:53.372 trial of Brentuximab in Jordan plus
NOTE Confidence: 0.82772666
00:51:53.372 --> 00:51:55.702 rituximab as frontline treatment for
NOTE Confidence: 0.82772666
00:51:55.702 --> 00:51:57.700 patients with immuno suppression
NOTE Confidence: 0.82772666
00:51:57.700 --> 00:52:00.175 associated lymphoma were presented and
NOTE Confidence: 0.82772666
00:52:00.175 --> 00:52:03.920 in the this was a very small study.
NOTE Confidence: 0.82772666
00:52:03.920 --> 00:52:07.360 22 patients with previously untreated
NOTE Confidence: 0.82772666
82
00:52:07.360 --> 00:52:08.736 immunosuppression associated.
NOTE Confidence: 0.82772666
00:52:08.740 --> 00:52:10.156 Little pretty effective disorder,
NOTE Confidence: 0.82772666
00:52:10.156 --> 00:52:11.926 including 1516 patients were PTSD
NOTE Confidence: 0.82772666
00:52:11.926 --> 00:52:13.449 post transplant clipart affective
NOTE Confidence: 0.82772666
00:52:13.449 --> 00:52:14.941 disorder patients who receive
NOTE Confidence: 0.82772666
00:52:14.941 --> 00:52:16.510 an induction were attacks.
NOTE Confidence: 0.82772666
00:52:16.510 --> 00:52:17.611 In other words,
NOTE Confidence: 0.82772666
00:52:17.611 --> 00:52:19.446 given in combination with Brent
NOTE Confidence: 0.82772666
00:52:19.446 --> 00:52:21.708 accidents and Odin and patient worry
NOTE Confidence: 0.82772666
00:52:21.708 --> 00:52:23.910 stage and according to their response,
NOTE Confidence: 0.82772666
00:52:23.910 --> 00:52:25.515 they either received more out
NOTE Confidence: 0.82772666
00:52:25.515 --> 00:52:27.639 attacks immigrant tax map in loading
NOTE Confidence: 0.82772666
00:52:27.639 --> 00:52:29.459 as consolidation and maintenance,
NOTE Confidence: 0.82772666
00:52:29.460 --> 00:52:32.064 or if they had progression of
NOTE Confidence: 0.82772666
00:52:32.064 --> 00:52:34.669 disease were removed from the study.
NOTE Confidence: 0.82772666
00:52:34.670 --> 00:52:35.906 Again, small study,
very short follow-up about encouraging result with a very high overall response rate, and see a rate of 60% so. I'm very excited to announce that we're about to open a phase two trial for this patient population here in the Yale network, and this is going to be a trial in collaboration with them. Are you clinic and with UVI so is just trial where patients with post transplant lymphoproliferative disorder CD 20 and CD 30 positive which essentially is the vast
The majority of PTSD will receive an induction treatment. Maximum burn toxin overload and then based on the response, they will receive more of the same treatment so and there will be spared cytotoxic treatment or will be escalated to rituximab, Pentax, Melvin Gordon, and Bendamustine, for a total of 6 cycles.

Primary objective of the study. Our overall response rate complete and partial at the end of the treatment and PFS secondary objective.
Additional responsibilities at the end of the induction phase, which include the grant axiom of windowed in on top of rituximab, duration of response and overall survival, and we’re planning to also deep dive into the frequency of infection. Peripheral sensory neuropathy, then rate doesn’t craft of interaction and treatment related mortality. Exploratory studies. Are at the end to identify new biological and genetic markers that might be productive to response resistance.
to this therapeutic combination.

NOTE Confidence: 0.779890875

So. Um?

NOTE Confidence: 0.779890875

I'm going to leave you with this last slide, future strategies and these are.

NOTE Confidence: 0.779890875

This is a list of the clinical trials

NOTE Confidence: 0.779890875

that are currently about to recruit

NOTE Confidence: 0.779890875

or recruiting for this for post

NOTE Confidence: 0.779890875

transplant lymphoproliferative disorder.

NOTE Confidence: 0.779890875

This top line is the study is our

NOTE Confidence: 0.779890875

study that I just mentioned and

NOTE Confidence: 0.779890875

we're about to open here at Yale

NOTE Confidence: 0.779890875

and then the reason I just want to

NOTE Confidence: 0.779890875

highlight the days a second study is.

NOTE Confidence: 0.74669033

Study that follows up the PLD

NOTE Confidence: 0.74669033

one trial from the German group,

NOTE Confidence: 0.74669033

whether increasing where they're
integrating the IPI score and the organ transplanted to further risk stratify patients after induction with rituximab and I have substituted rituximab subcu to the regular attacks enough that they used in the PTL D1 trial. Another trial that I would keep an eye on is there tax amount plus a club routine atrial that is not yet recruiting and is going to be done in Cleveland and besides this retrial which address the untreated population in the refractory setting, there are a lot of trials with the adoptive T cell treatment.
And with this and this, is it? So thank you for your attention.

Thank you, that was a wonderful talk and it’s great to see that you have a trial and I guess it’s opening Greninger will be.

So very very well linked to the first talk we heard from Ann.

Do you have any questions or comments where we’re just about a time, but we might have time for one or two?

Are you seeing a lot of this in your practice right now?

Princeska in Greenwich?

Currently have one patient which is,
which is a lot considering that I’ve just started two months ago. So we have we typically used to have. Colombia is a big transplant center and we we tend to. We were seeing a lot of these patients, but to say a lot was about 20-30 cases per year. Just to put this in context, so this is a rare disease weapon. As we grow Greenwich as a expert site, you know for these types of diseases you’ll get you’ll draw more and more from Manhattan, and where I’m sure there are
many post transplant patients,
Francine Flash has a question. She asks any role for checkpoint inhibitors in these EBV driven tumors. This is a very good question and I think that due to the peculiarity of these patients population, which are recipients of hematopoietic stem cell transplant or solid organ transplant, there is a lot of. We're very worried about causing it'd have to be action or graft versus host disease, and so I don’t. I'm not aware of any study utilizing checkpoint inhibitors in this specific patient population.
OK, maybe I see a study in the making,
maybe an investigator initiated trial.
Well, our Francisco that was great.
Thank you so much.
Welcome to the group you’ve.
It’s great to have you and this
will end grand rounds for today.
I want to thank Renee and her team
for helping get this set up and I hope
everyone has a good rest of the day.
Will see you soon.
Thank you, thanks everyone.