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 actually ends very much in the news today.

Congratulations.

And so an is associate Professor of Medicine, and an is associate Professor of Medicine, medical oncology and Deputy Chief medical Officer for Smile Cancer hospital.

Congratulations.

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
00:01:05.958 --> 00:01:07.598 efforts in clinical research,
NOTE Confidence: 0.80177414
00:01:07.600 --> 00:01:08.731 adult care centers.
NOTE Confidence: 0.80177414
00:01:08.731 --> 00:01:10.993 She's a particular focus in quality
NOTE Confidence: 0.80177414
00:01:10.993 --> 00:01:12.496 measurement and improvement and
NOTE Confidence: 0.80177414
00:01:12.496 --> 00:01:14.626 his work to achieve ASCO copy
NOTE Confidence: 0.80177414
00:01:14.626 --> 00:01:16.217 certification for the entire smell.
NOTE Confidence: 0.80177414
00:01:16.220 --> 00:01:17.294 Academic clinical practice
NOTE Confidence: 0.80177414
00:01:17.294 --> 00:01:18.368 of actually received.
NOTE Confidence: 0.80177414
00:01:18.370 --> 00:01:20.170 Actually, the Joe Simone Award,
NOTE Confidence: 0.80177414
00:01:20.170 --> 00:01:22.676 just recently in Q just passed away
NOTE Confidence: 0.80177414
00:01:22.676 --> 00:01:25.548 last week, but a big honor for Masco,
NOTE Confidence: 0.80177414
00:01:25.550 --> 00:01:27.944 so an it’s a pleasure to have
NOTE Confidence: 0.80177414
00:01:27.944 --> 00:01:30.278 you here for our first talk.
NOTE Confidence: 0.80177414
00:01:30.280 --> 00:01:32.192 Transformation in quality building
NOTE Confidence: 0.80177414
00:01:32.192 --> 00:01:33.626 a cancer network,
NOTE Confidence: 0.80177414
00:01:33.630 --> 00:01:34.100 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.

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
NOTE Confidence: 0.8790028
00:02:47.632 --> 00:02:49.458 individually next to each other,
NOTE Confidence: 0.8790028
00:02:49.460 --> 00:02:51.818 but somehow there was a transformation
NOTE Confidence: 0.8790028
00:02:51.818 --> 00:02:53.892 of the individual stands into
NOTE Confidence: 0.8790028
00:02:53.892 --> 00:02:55.640 a different collective entity,
NOTE Confidence: 0.8790028
00:02:55.640 --> 00:02:56.464 real community,
NOTE Confidence: 0.8790028
00:02:56.464 --> 00:02:59.760 and so in the same way that in
NOTE Confidence: 0.8790028
00:02:59.760 --> 00:03:02.592 the same way I want to talk about
NOTE Confidence: 0.8790028
00:03:02.592 --> 00:03:05.119 cancer or cancer network today,
NOTE Confidence: 0.8790028
00:03:05.120 --> 00:03:07.190 there really has been a trend
NOTE Confidence: 0.8790028
00:03:07.190 --> 00:03:10.186 over the past 10 years of academic
NOTE Confidence: 0.8790028
00:03:10.186 --> 00:03:12.741 institutions or other entities buying
NOTE Confidence: 0.8790028
00:03:12.741 --> 00:03:16.018 up practices or putting up their names on.
NOTE Confidence: 0.8790028
00:03:16.020 --> 00:03:16.802 Affiliated practices,
NOTE Confidence: 0.8790028
00:03:16.802 --> 00:03:19.930 but what I wanted to focus on is
NOTE Confidence: 0.8790028
00:03:20.003 --> 00:03:22.635 how to how I think we’ve built
NOTE Confidence: 0.8790028
00:03:22.635 --> 00:03:24.420 a real transformative network,
00:03:24.420 --> 00:03:26.826 a community that is better than
00:03:26.826 --> 00:03:29.035 the individual units where cancer
00:03:29.035 --> 00:03:31.685 delivery is really somehow transformed.
00:03:31.690 --> 00:03:34.108 And so you know, this is,
00:03:34.110 --> 00:03:36.630 let’s go to transformation theory too
00:03:36.630 --> 00:03:39.369 as a guiding principle for this work.
00:03:39.370 --> 00:03:40.579 As it is,
00:03:40.579 --> 00:03:42.997 Carter said transformation is a process,
00:03:43.000 --> 00:03:44.032 not an event.
00:03:44.032 --> 00:03:46.440 And you start with a sense of
00:03:46.524 --> 00:03:49.116 urgency form a coalition and you
00:03:49.116 --> 00:03:51.490 create and share that vision.
00:03:51.490 --> 00:03:54.714 You empower others to act on that vision.
00:03:54.720 --> 00:03:57.138 You plan, create short term wins,
00:03:57.140 --> 00:03:58.352 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 had 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. 9 1/2 years later the this. This is our clinical footprint in Connecticut and in Rhode Island. This stars are where our 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 AC OS, 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 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 practices and in terms of improving our process and improving our onboarding process and now as I said...
we have 15 locations in two states.

We have almost 50 MD's, 16 aips and over 400 staff we see over 9000 new patients yearly 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 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,
work which were very useful.
On an ongoing are useful on an ongoing basis.
We developed a formal onboarding curriculum,
and this utilized leaders and peers
is faculty and it really included
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?
NOTE Confidence: 0.8576237

How does the research apparatus work?
NOTE Confidence: 0.8576237

Who are the dart leaders?
NOTE Confidence: 0.8576237

What is that mean?
NOTE Confidence: 0.8576237

What is what are academic mentors and and?
NOTE Confidence: 0.8576237

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.
NOTE Confidence: 0.8165863

What is what are academic mentors and and?
NOTE Confidence: 0.8165863

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.
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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 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. Go up to 90 metrics of oncology
of ambulatory oncology, quality that have been developed national iyanar consensus based and evidence based when available, so we had a measurement at baseline. Representing the practices before they joined and then this is four years later we looked at the significant differences and saw that really the only changes were in the positive. These are actually shown here and and these were really important to me because I wanted to make sure again it wasn’t just putting in a sign on the door, but that we were actually using.
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 logistics around dialing in, presented and so you can see in 2013. This was difficult because the logistics around dialing in,
00:12:46.150 --> 00:12:49.494 which is so easy now by assume it.
NOTE Confidence: 0.80547464
00:12:49.500 --> 00:12:52.440 But at that time was very difficult.
NOTE Confidence: 0.80547464
00:12:52.440 --> 00:12:55.860 Getting the path reviewed, getting the.
NOTE Confidence: 0.80547464
00:12:55.860 --> 00:12:58.305 Radiology diagnostic imaging to be
NOTE Confidence: 0.80547464
00:12:58.305 --> 00:13:01.555 available that was really hard at the
NOTE Confidence: 0.80547464
00:13:01.555 --> 00:13:04.082 time and now I think we’ve received
NOTE Confidence: 0.80547464
00:13:04.082 --> 00:13:06.858 we’ve we’ve sort of the steady state,
NOTE Confidence: 0.80547464
00:13:06.860 --> 00:13:08.548 is right around 500.
NOTE Confidence: 0.80547464
00:13:08.548 --> 00:13:10.236 That’s the case also.
NOTE Confidence: 0.80547464
00:13:10.240 --> 00:13:12.360 Sorry, this is 2018-2019, 2020,
NOTE Confidence: 0.80547464
00:13:12.360 --> 00:13:14.470 right around the 500 mark,
NOTE Confidence: 0.80547464
00:13:14.470 --> 00:13:17.640 which I think represents sort
NOTE Confidence: 0.80547464
00:13:17.640 --> 00:13:20.176 of the steady state.
NOTE Confidence: 0.80547464
00:13:20.180 --> 00:13:22.700 Um, with respect to customer service.
NOTE Confidence: 0.80547464
00:13:22.700 --> 00:13:26.330 Those of you who have.
NOTE Confidence: 0.80547464
00:13:26.330 --> 00:13:27.084 You know,
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. This highlights some of the innovative projects that we’ve taken on in the network.
This was a pilot with Asko Asko has a quality training program that is 6 months and has three didactic sessions and and a very aggressive curriculum every two weeks around process mapping and barrier analysis and ultimately multiple PDS a cycles. In this case, we had a team from every care center at the time in 2000. and we did it again, and in one case in MA Pharmacy to conduct quality improvement and all of those groups were
able to complete at least one PDS, a cycle over two years or each year, each year getting through. Ipedia say cycle and this work ultimately resulted in nine story in five national presentations, and 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 and what they 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 QI to better care, recognize opportunities to reuse them to face challenges 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’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 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.

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, 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. About 50% cooperative group, 43% industry sponsored in 10% IIT’s. Here you see that 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 guess 900 sites across the US in 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 this trial I think will tell us. Very important.
00:22:30.900 --> 00:22:33.567 Give us information on sequencing of chemo.
NOTE Confidence: 0.8432984

00:22:33.570 --> 00:22:35.850 If you can spare it upfront.
NOTE Confidence: 0.8432984

00:22:35.850 --> 00:22:38.076 If you add it to the immunotherapy if that will help.
NOTE Confidence: 0.8432984

00:22:38.076 --> 00:22:40.040 And ultimately because we are collecting tissue from this trial,
NOTE Confidence: 0.8432984

00:22:40.040 --> 00:22:41.945 we're going to be looking for prognostic signatures for Pember Lizum.
NOTE Confidence: 0.8432984

00:22:41.945 --> 00:22:43.850 This is also an IIT of mine in small cell which with the biopsy upfront.
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00:22:43.850 --> 00:22:46.436 and then on treatment at week four after treatment with EPI,
NOTE Confidence: 0.8432984

00:22:46.436 --> 00:22:48.650 and on treatment at week four.
NOTE Confidence: 0.8432984

00:22:48.650 --> 00:22:50.735 This is also an IIT of mine in small cell which with the biopsy upfront.
NOTE Confidence: 0.8432984

00:22:50.735 --> 00:22:53.450 This is also an IIT of mine in small cell which with the biopsy upfront.
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00:22:53.450 --> 00:22:56.609 and then on treatment at week four after treatment with EPI,
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00:22:56.609 --> 00:22:59.365 and then on treatment at week four after treatment with EPI,
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00:23:02.769 --> 00:23:05.279 and then on treatment at week four after treatment with EPI,
NOTE Confidence: 0.8432984

00:23:05.280 --> 00:23:08.346 and then on treatment at week four after treatment with EPI,
NOTE Confidence: 0.8432984

00:23:08.346 --> 00:23:11.978 and then on treatment at week four after treatment with EPI,
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 lits 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 folfoxin.
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 D clinics and that some of the work that I'm going to carry on in my integration role and strengthen our alignment with disease teams. And certainly our disease centers to 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 not numbers of patients, but really I think the faculty that have
joined his care center is one of them.

Francesca is going to give a grand rounds right after me.

They all master clinicians.

They have devoted their really the clinical arm of a female cancer and smilow cancer hospital within the community and all have joined with the disease teams to do you know any number of really exciting things.

BPI on trials do collaborative research projects, develop Qi projects, help teaching our house staff and anymore so it has really been my 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 effort of many, many hands to build the network, including Charlie and Lori. Kevin Billingsley, Aleesa Chomsky, Monica Fradkin, Connie Engelking, Roy Herbst, and 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 process.
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 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,
so I will just follow up and say no.

Make it secure.

Diverse state as you go up and down the 95 corridor.

How are we trying to help increase the diversity of our patient population at our care centers to get more patients from diverse backgrounds on trials?

That’s certainly something that we can now do that we have so much integration within the state.

Great great great question.

I’m just going to go back and share my screen again so you can see who’s doing a lot of this work.
You know, Melinda, that’s a 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, one of her passions is increasing representation of under addressing disparities of care, in clinical trials and addressing disparities of care, and she’s done a number of things, including that 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 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 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 I'll mention you know again, Melinda's talked. I didn't talk about the 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 you know attempts to understand the science behind that. 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.

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

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, 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
NOTE Confidence: 0.83359927
00:31:23.364 --> 00:31:25.488 lymphoproliferative disorders franceska.
NOTE Confidence: 0.89172757
00:31:27.850 --> 00:31:30.310 Thank you for the introduction,
NOTE Confidence: 0.89172757
00:31:30.310 --> 00:31:32.770 so I'll share my screen.
NOTE Confidence: 0.7702043
00:31:37.680 --> 00:31:40.707 OK, so good afternoon everybody.
NOTE Confidence: 0.7702043
00:31:40.707 --> 00:31:44.421 I will review today was transparently
NOTE Confidence: 0.7702043
00:31:44.421 --> 00:31:45.930 proliferative disorders.
NOTE Confidence: 0.7702043
00:31:45.930 --> 00:31:49.759 So here's my disclosures. So we are.
NOTE Confidence: 0.7702043
00:31:49.760 --> 00:31:53.491 We will review together and how PLD
NOTE Confidence: 0.7702043
00:31:53.491 --> 00:31:56.308 are classified according to the
NOTE Confidence: 0.7702043
00:31:56.308 --> 00:31:58.560 most recent WHL classification,
NOTE Confidence: 0.7702043
00:31:58.560 --> 00:32:01.310 the Epidemiology, the risk factors
NOTE Confidence: 0.7702043
00:32:01.310 --> 00:32:04.060 at timing of onset prognosis,
NOTE Confidence: 0.7702043
00:32:04.060 --> 00:32:06.260 and therapeutic options including
NOTE Confidence: 0.7702043
00:32:06.260 --> 00:32:08.460 a current treatment paradigms,
NOTE Confidence: 0.7702043
00:32:08.460 --> 00:32:11.220 ongoing clinical trials and
NOTE Confidence: 0.7702043
50
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 T cell nail Plaza and the classical Hodgkin lymphoma. So purely nondestructive, these diseases are classified based on the pathology major.
findings and under sell 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,
with the associated to a large area of necrosis and on the right variable size and shape lymphoid infiltrate.

Monomorphic PTSD, those are the one that do fulfill the criteria for non Hodgkin lymphoma or plasma cell neoplasm, small B cell lymphoma are not considered at not the designated as PTLT,

Hodgkin lymphoma or plasma cell neoplasm, extranodal marginal zone lymphoma that usually arise in the cutaneous or subcutaneous tissue and this is because their standardized incidence ratio is not different than in the regular population and they’re not started to happen.

As a consequence of the immune suppression,
NOTE Confidence: 0.80955
00:35:21.770 --> 00:35:24.826 besides those any other kind of non Hodgkin lymphoma is considered uppity ality.
NOTE Confidence: 0.80955
00:35:24.826 --> 00:35:27.330 So the architecture defacement is usually present.
NOTE Confidence: 0.80955
00:35:28.910 --> 00:35:30.095 Immuno, phenotypic and genetic features are typically recapitulating what we do see individual competent counterpart.
NOTE Confidence: 0.80955
00:35:30.100 --> 00:35:32.025 And here I included an example on the left of.
NOTE Confidence: 0.80955
00:35:32.025 --> 00:35:34.415 You should be selling for infiltrating. Lymph node and underwrite dereza.
NOTE Confidence: 0.80955
00:35:34.415 --> 00:35:36.039 This is a renal allograft biopsy with the planning T cell gamma,
NOTE Confidence: 0.80955
00:35:36.040 --> 00:35:39.376 Delta, An example.
NOTE Confidence: 0.80955
00:35:39.376 --> 00:35:41.600 This is a renal allograft biopsy with the 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 mixedcellularity.

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 a 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.

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 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 with a higher risk followed by lung,

heart, liver, pancreas and with kidney being the carrying the lower risk for multiple attic stem cell transplant.

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
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.
00:39:43.091 --> 00:39:45.828 factor for development of these
NOTE Confidence: 0.8300465
00:39:45.828 --> 00:39:48.160 diseases and the conditioning.
NOTE Confidence: 0.8300465
00:39:48.160 --> 00:39:53.720 Regiment. Um also, um.
NOTE Confidence: 0.8300465
00:39:53.720 --> 00:39:55.900 So in terms of timing,
NOTE Confidence: 0.8300465
00:39:55.900 --> 00:39:58.115 typically PTSD arrives early in
NOTE Confidence: 0.8300465
00:39:58.115 --> 00:40:00.330 the setting of hematopoetic stem.
NOTE Confidence: 0.8300465
00:40:00.330 --> 00:40:02.622 The transplant and leader in the
NOTE Confidence: 0.8300465
00:40:02.622 --> 00:40:05.500 setting of a solid organ transplant,
NOTE Confidence: 0.8300465
00:40:05.500 --> 00:40:08.086 but it’s not really that predictable.
NOTE Confidence: 0.8300465
00:40:08.090 --> 00:40:10.904 We considered an early onset if PTSD arises in the first year after
NOTE Confidence: 0.8300465
00:40:10.904 --> 00:40:16.705 the transplant and the late onset,
NOTE Confidence: 0.8300465
00:40:16.710 --> 00:40:19.290 if it arises a year later.
NOTE Confidence: 0.8300465
00:40:19.290 --> 00:40:24.197 Starting one year after the transplant and.
NOTE Confidence: 0.8300465
00:40:24.200 --> 00:40:26.280 And the reason the battle,
NOTE Confidence: 0.8300465
00:40:26.280 --> 00:40:28.860 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
specimen link to clinical information, and this is what we have learned from the analysis of 120 patients. This is the largest series published so far on this specific disease. Interestingly, most of the clinical features that we think might predict an outcome might have an impact on the overall survival. Did not correlate with overall survival in our patient population, including the subtype of the PTSD, the decade of diagnosis prior or after the introduction of their attack.
Some organ do kind of organ transplanted

DV status, graft involvement,

and extranodal involvement

or stage of diagnosis.

So using a recursive partitioning model,

we separated patient.

Recursively,

at each step into two distinct

groups based on the variables that

provided the maximal separation based

on survival and using this model,

we were able to identify based on

age CD 20 expression and equal status

for groups that were well separated

in terms of roll survival and with

an even number of patient and in 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 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
00:44:04.899 --> 00:44:07.969 cell type and all T cell period in
00:44:07.969 --> 00:44:10.689 our series were leaving negative.
00:44:10.690 --> 00:44:13.539 Another thing that we have
00:44:13.539 --> 00:44:16.775 also learned is that importance of more
00:44:16.775 --> 00:44:19.661 marrow of staging and the incidents
00:44:19.746 --> 00:44:22.518 of more involvement in the in PLD.
00:44:22.520 --> 00:44:26.056 It is very common in our series of
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
00:44:31.570 --> 00:44:35.030 in the in the T cell subtypes 50%.
00:44:35.030 --> 00:44:35.514 Also,
00:44:35.514 --> 00:44:37.450 polymorphic exhibited our very
00:44:37.450 --> 00:44:39.386 high bone marrow involvement.
00:44:39.390 --> 00:44:42.393 15.7 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 trajaenic

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 as we saw there is a bigot originality in the type of PTSD that is it originality in the patient population, in the allograft or multiply attic stem cell transplant, 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
with a toddler stem cell transplant or both being explored. So there are only few prospective trials, primarily on polymorphic and monomorphic beissel. PTSD and hold the. Stop for trials here. Use their attack some as a single agent with a very high with a good overall response rate under an CR rate, but not exciting overall survival due to early relapse is the best results that have been achieved that utilizing either a sequential treatment or a risk stratifies sequential treatment and this is the
The largest phase two trial ever conducted in this patient population and reported by the German study group will review the results of the PD L D1. The risk stratified sequential treatment was published in JCO in 2017. Patients with newly diagnosed PTSD received an induction treatment with rituximab and then based on their response, they received consolidation with rituximab alone or were escalated to CHOP. 152 patients were enrolled again.
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
NOTE Confidence: 0.82772666
00:50:12.820 --> 00:50:14.080 this is a attribute.
NOTE Confidence: 0.82772666
00:50:14.080 --> 00:50:16.114 This has been attributed to the
NOTE Confidence: 0.82772666
00:50:16.114 --> 00:50:18.998 fact that a quarter of the patients
NOTE Confidence: 0.82772666
00:50:18.998 --> 00:50:20.938 were spared cytotoxic chemotherapy.
NOTE Confidence: 0.82772666
00:50:20.940 --> 00:50:24.210 So. What’s new in PID.
NOTE Confidence: 0.82772666
00:50:24.210 --> 00:50:26.245 Recently over the past five
NOTE Confidence: 0.82772666
00:50:26.245 --> 00:50:29.196 years it has been more and more
NOTE Confidence: 0.82772666
00:50:29.196 --> 00:50:31.698 recognized than PTSD tend to be.
NOTE Confidence: 0.82772666
00:50:31.700 --> 00:50:35.860 CD 30 positive So this is a study by vision.
NOTE Confidence: 0.82772666
00:50:35.860 --> 00:50:38.164 Others that showed that out of
NOTE Confidence: 0.82772666
00:50:38.164 --> 00:50:40.242 108 patients with PTSD diagnosed
NOTE Confidence: 0.82772666
00:50:40.242 --> 00:50:43.375 between 1994 and 2011, it was 85%.
NOTE Confidence: 0.82772666
00:50:43.375 --> 00:50:46.350 Of this patient expresses CD 30 including
NOTE Confidence: 0.82772666
00:50:46.439 --> 00:50:49.585 81% of the diffuse large B cell lymphoma.
NOTE Confidence: 0.82772666
00:50:49.590 --> 00:50:52.030 This is very particular to
NOTE Confidence: 0.82772666
00:50:52.030 --> 00:50:54.470 the query after the PTLD.
NOTE Confidence: 0.82772666
00:50:54.470 --> 00:50:55.990 Because in the immunocompetent,
NOTE Confidence: 0.82772666
00:50:55.990 --> 00:50:58.270 if you started selling for my
NOTE Confidence: 0.82772666
00:50:58.338 --> 00:51:00.243 usually city third expression is
NOTE Confidence: 0.82772666
00:51:00.243 --> 00:51:02.919 probably less than 20% and not only
NOTE Confidence: 0.82772666
00:51:02.919 --> 00:51:05.217 demonstrated a high CD 30 expression.
NOTE Confidence: 0.82772666
00:51:05.220 --> 00:51:07.776 They also demonstrated that it was
NOTE Confidence: 0.82772666
00:51:07.776 --> 00:51:10.735 associated with a better outcome. So.
NOTE Confidence: 0.82772666
00:51:10.735 --> 00:51:13.760 Twice this interesting or important,
NOTE Confidence: 0.82772666
00:51:13.760 --> 00:51:16.770 we now have a drug that targets
NOTE Confidence: 0.82772666
00:51:16.770 --> 00:51:19.220 specifically city 30 brentuximab windowed
NOTE Confidence: 0.82772666
00:51:19.220 --> 00:51:22.442 and is an antibody drug conjugate
NOTE Confidence: 0.82772666
00:51:22.442 --> 00:51:25.509 that binds to the city 30 and one.
NOTE Confidence: 0.82772666
00:51:25.510 --> 00:51:27.410 Since the internalised release,
NOTE Confidence: 0.82772666
00:51:27.410 --> 00:51:29.785 monumental restarting E which is
NOTE Confidence: 0.82772666
00:51:29.785 --> 00:51:31.573 microtubule disrupting agent which
end up like causing apoptosis.

As we all know, grant access method Odin is now approved with various indications in Hodgkin lymphoma anaplastic large. Calling from.

So in 2019, at the ASH meeting, the results of these Phase 1 two trial of Brentuximab in Jordan plus rituximab as frontline treatment for patients with immuno suppression were presented and in the this was a very small study. 22 patients with previously untreated
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, 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
00:53:11.530 --> 00:53:13.590 majority of PTSD will receive
NOTE Confidence: 0.82772666
00:53:13.590 --> 00:53:15.238 an induction treatment with.
NOTE Confidence: 0.82772666
00:53:15.240 --> 00:53:17.155 Maximum burn toxin overload and
NOTE Confidence: 0.82772666
00:53:17.155 --> 00:53:19.551 and then based on the response
NOTE Confidence: 0.82772666
00:53:19.551 --> 00:53:21.969 at a pet city after induction,
NOTE Confidence: 0.82772666
00:53:21.970 --> 00:53:24.469 they will receive more of the same
NOTE Confidence: 0.82772666
00:53:24.469 --> 00:53:27.126 treatment so and there will be spared
NOTE Confidence: 0.82772666
00:53:27.126 --> 00:53:29.394 of cytotoxic treatment or will be
NOTE Confidence: 0.82772666
00:53:29.468 --> 00:53:31.476 escalated to rituximab, Pentax,
NOTE Confidence: 0.82772666
00:53:31.476 --> 00:53:33.060 Melvin Gordon, and Bendamustine,
NOTE Confidence: 0.82772666
00:53:33.060 --> 00:53:35.436 for a total of 6 cycles.
NOTE Confidence: 0.82772666
00:53:35.440 --> 00:53:37.420 Primary objective of the study.
NOTE Confidence: 0.82772666
00:53:37.420 --> 00:53:39.280 Our overall response rate complete
NOTE Confidence: 0.82772666
00:53:39.280 --> 00:53:42.050 and partial at the end of the
NOTE Confidence: 0.82772666
00:53:42.050 --> 00:53:44.150 treatment and PFS secondary objective.
NOTE Confidence: 0.82772666
00:53:44.150 --> 00:53:45.419 Intend to explore.
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. At the end to identify new biological and genetic markers that might be productive to response resistance.
to this therapeutic combination.

So. Um?

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

This is a list of the clinical trials that are currently about to recruit or recruiting for this for post transplant lymphoproliferative disorder.

This top line is the study is our study that I just mentioned and we're about to open here at Yale.

Study that follows up the PLD one trial from the German group, 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? If there are any.

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 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.