Welcome again to Cancer Center.

Grand rounds, good afternoon and as is often the case, we have some really exciting data and progress and science and clinical care to share with you in this.

The theme for today, which is a really interesting one and different because we have multiple speakers, is in hematology where we’ve made enormous progress.

And we’re both biology translational work, population science and clinical care in
the major hematologic latency is leukemia and myeloid malignancy’s lymphoma. Multiple myeloma where I think we have really talented people working on these problems and really translating science into progress for our patients and looking forward to all four presentations. But I will actually turn to our leader and host for essentially, our leader and host for the session to make the introductions, so I’ll start simply by introducing Doctor Stephanie Allyne. As you know, Stephanie is the chief of hematology at Yale, as well as an associate
professor of medicine.

In addition, Stephanie Overseas the DeLuca Center for Innovation and Hematology Research, which is really an exciting addition to our work in hematology, with the promise that not only translating our discoveries into clinical care innovation. But also in furthering the support of our faculty and trainees. Stephanie joined the faculty in Yale in 2006. An we were so pleased that she was selected as our new Chief in 2020 and is doing a great job and looking forward to her an our faculty.
00:01:59.543 --> 00:02:02.090 sharing the exciting work at Yale.

00:02:02.090 --> 00:02:04.580 So Stephanie I turn to you.

00:02:06.650 --> 00:02:08.140 Let me share my slides.

00:02:11.490 --> 00:02:13.940 OK, can you see the slides well?

00:02:14.855 --> 00:02:16.380 Alright, let’s tally Saturday will preside,

00:02:16.380 --> 00:02:17.905 present or represent on translational science and hematology.

00:02:20.960 --> 00:02:23.696 so I will be the one driving the slide.

00:02:23.700 --> 00:02:25.960 So any hiccups blame me.

00:02:25.960 --> 00:02:27.316 Um, so I’ll be.

00:02:27.316 --> 00:02:29.350 I’ll be giving a brief introduction

00:02:29.417 --> 00:02:31.507 to hematology and then tomorrow

00:02:31.507 --> 00:02:33.597 probably will present on behalf

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00:02:33.671 --> 00:02:36.161 of the myeloid malignancies team
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00:02:36.161 --> 00:02:37.655 and traumatizing associate,
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00:02:37.660 --> 00:02:38.974 professor of medicine,
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00:02:38.974 --> 00:02:39.412 hematology,
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00:02:39.412 --> 00:02:42.511 and he’s a director of the MLP
NOTE Confidence: 0.87615436
00:02:42.511 --> 00:02:44.091 malignancies disease team and
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00:02:44.091 --> 00:02:46.859 the firm chief of the data firm,
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00:02:46.860 --> 00:02:49.050 and everybody knows just how
NOTE Confidence: 0.87615436
00:02:49.050 --> 00:02:51.702 much moving Anan changes had to
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00:02:51.702 --> 00:02:54.006 happen over the past years to
NOTE Confidence: 0.87615436
00:02:54.006 --> 00:02:56.389 keep our clinical services alive.
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00:02:56.390 --> 00:02:58.754 And to my actually completed his
NOTE Confidence: 0.87615436
00:02:58.754 --> 00:03:01.840 doctor rent in medical hematology oncology.
NOTE Confidence: 0.87615436
00:03:01.840 --> 00:03:04.150 Myung then joined the Paoli
NOTE Confidence: 0.87615436
00:03:04.150 --> 00:03:05.998 Calmettes’s Institute in Marseille
NOTE Confidence: 0.87615436
00:03:05.998 --> 00:03:08.715 and did a full ride scholarship
at Johns Hopkins University, and I think that’s how eventually he landed with us. With Steve Gore recruiting him. After tomorrow, Doctor Francine Foss, Professor of Medicine and hematology and Rheumatology, would present on behalf of the former team and. Francine really is the expert in T cell lymphoma, internationally, nationally, renown, and she’s a research director of an informal disease team and obviously director of the Tucson Informer program.
and you will hear exciting news what is happening in the format to selling Thelma and last but not least, doesn’t Italian infrared, so will present on behalf of the multiple myeloma disease team. And she’s the research director of the much more disease team and an assistant professor in. Medicine medical oncology. She actually obtained her medical degree in Tennessee and the country of Georgia, then did postdoctoral fellowships at Emory Northwestern and Lucky for us a deal. She did her residency and fellowship. Odicle refill Oscar left us,
but we were able to recruit her back to be part of the team.

So um, before I introduce much about hematology, I think it’s absolutely time that we all say thank you to Charlie. So Charlie, you took over as our interim section Chief in January 2018 and has been a just wonderful, wonderful journey since then. So you can see just how big the group is in hematology and growing. And I just want to read a few of the quotes from our faculty.
And that is so Charlie,

you recognize the strength,

resilience and enthusiasm in

the new teologi faculty, staff,

advanced practice providers,

nurses entry needs,

and you supported our teams in so many ways.

Thank you for the leadership and

commitment you provided as interim Chief.

Your strong support and advocacy

for our section is not appreciated.

Thank you for being an outstanding

leader and role model for trainees

through your dedication to

excellence in patient care,

teaching and innovation.
It has been an honor to learn from you and the excellent faculty of your Cancer Center and thank you for everything you’ve done for the Cancer Center and was a section of hematology over the past several years. You have been a wonderful resource and a guide from my academic growth, and I’m extremely grateful to you. So thank you, Charlie. Thank you in the entire division. It’s a real point of pride to me to have been a member and now along of this very August center of excellence. So thank you.
And we have a little bit more in store, so the thing we really wanted to thank you for is how you have supported all our people and recruitment of all these people highlighted in yellow. You know Murrayshall is to my like. Barbona is our director of classic hematology, Sabrina Browning as a member of our myeloma and come up as a team. And as you can see, also of our billing team. And then in addition to that, you have recruited hematology focused faculty to the to the Smiler.
network and the care centers,

And we’re so fortunate to work with all our colleagues.

And of course Mike’s mission as a director of the Center for Molecular and Cellular.

I always say hematology and oncology in there were so excited about,

you know, all our new people and teams

I say core because these are the people located in New Haven,
North Haven.

And these are the teams that are working hard to bring the best patient care to all patients in Connecticut and beyond through their research.

So we have five teams in my life. Five is all the teams we have smile. Oh yeah, even health and University. So we have five teams in my life.

Wendell Smith. We call it classical hematology because as we all know. Behind him, disorders are not that denied. Our patients are quite ill and then our
minds from my Loma and commodities team.

So as I mentioned before, we're not alone. We're not just a small, tiny little point on the map in New Haven, but through our smaller network we have reached across the entire state and it is just wonderful to know that we can bring the excellent signs and treatment to all patients in Connecticut. Then again, here I'm highlighting our hematology focused faculty, which is also new over the last several years and it’s just wonderful.
How much team building can we do?

There are many discussions already going on between our disease team leaders and faculty and tremble in North Haven, Guilford, Hardford and all the other places. So it’s wonderful opportunity. Um, we’re not alone and we’re not doing this in isolation, so we’re fortunate to be at a place like here where there are many different centers there. We have our Decker Jews tallied in the clinical Trials Office. Again, again,
Bosenberg leading yell center. Female oncologist Mark Lemon, leading the year Cancer Biology Institute kinda Neugebauer, leading the Larne Center. And then Diane Krause in the my C Age and then cheers of the different departments. Chengdu for pathology. We have collaborators in the stem cell center. We have collaborators in the copper center. Marcella Nunez Smith just gave a talk to the leaders this morning.
and Antonio riders and many, many more that I can't even get on this slide.

So, um, I just wanted to give a brief update on the Delucas Center for Innovation and Hematology Research, another amazing initiative that Charlie made happen and we are now have just riding our progress report for the past two years and just to give you an update. So we have a very active hematology tissue bank with samples from patients with all human logic disorders. We have over 4000 samples from over 2000 Nations, we have a bone marrows prefer blood. We’re working also collecting lymph.
node tissue and other tissue biopsies.

And we also offer specialized processing for clinical trials in hematology.

And this is again a huge.

Team effort so you see our core people on the right and Michelle Patel, rounder, Feli, Padma Mamillapalli and our latest recruit Jennifer from donor Hoban.

But everybody in hematology is contributing to this.

All our aips an MP7 in North Haven at Trumbull.

Another care centers and we hope to leverage this tissue bank to better understand
these users and offering treatments.

We have awarded 9 pilot grants or $50,000 each.

Our goal is to have these being through these be collaborative between collisions and basic scientists.

We have one career development award E chaining cathari. These are two year awards and the our base posted for new applicants. We have many many applications

This data that eventually will allow
00:10:58.196 --> 00:11:00.190 clinician scientists in a deidentified manner screen what we have in the database so they can come up with ideas and let us know how we can help them.

00:11:00.190 --> 00:11:02.745 We’re providing access to novel technologies.

00:11:02.745 --> 00:11:05.173 Jennifer Amisha Jazz performed single site DNA sequencing for clinical trial samples for Maccabean.

00:11:05.173 --> 00:11:08.000 We have many more ideas and we are also seeking to provide Technical Support for correlative studies and data analysis.

00:11:08.000 --> 00:11:10.076 So let me now go over to the disease teams, so this these are the members of the stem cell transplantation cellular therapies team, but they will not present today.

20
00:11:34.092 --> 00:11:36.590 because you should stay tuned and log
NOTE Confidence: 0.84497094
00:11:36.590 --> 00:11:38.708 into the Young Cancer Center grounds.
NOTE Confidence: 0.84497094
00:11:38.710 --> 00:11:41.038 I think it’s March 23rd when
NOTE Confidence: 0.84497094
00:11:41.038 --> 00:11:43.645 Doctor Supinder for her with her
NOTE Confidence: 0.84497094
00:11:43.645 --> 00:11:45.589 present on cellular therapies.
NOTE Confidence: 0.84497094
00:11:45.590 --> 00:11:48.019 You will also not here today from
NOTE Confidence: 0.84497094
00:11:48.019 --> 00:11:49.420 our classical hematology team,
NOTE Confidence: 0.84497094
00:11:49.420 --> 00:11:51.075 because Doctor Boner just presented
NOTE Confidence: 0.84497094
00:11:51.075 --> 00:11:53.589 not so long ago in grand rounds.
NOTE Confidence: 0.84497094
00:11:53.590 --> 00:11:55.984 But we’re also very hopeful to getting
NOTE Confidence: 0.84497094
00:11:55.984 --> 00:11:59.159 a slot in the summer when we will have,
NOTE Confidence: 0.84497094
00:11:59.160 --> 00:12:00.548 hopefully exciting new recruits
NOTE Confidence: 0.84497094
00:12:00.548 --> 00:12:02.283 to add to the team.
NOTE Confidence: 0.84497094
00:12:02.290 --> 00:12:04.838 And we can take a full grand
NOTE Confidence: 0.84497094
00:12:04.838 --> 00:12:07.630 rounds for our classic hematology.
NOTE Confidence: 0.84497094
00:12:07.630 --> 00:12:10.555 So the team you will be hearing from today.
The first one is on myeloid malignancy’s team and Doctor Priebe will present on behalf of this group and so now I’m heading over to Doctor Kirby for the first presentation. Within blessed to have already Nikolai in myself. Within single, fewer a few weeks ago on this ground round and I guess that you know probably most of the members of the team already. That on our side and that any color without self on universe recruit Rory share is.
00:12:45.560 --> 00:12:47.545 Doctor Brokaw from San Francisco
NOTE Confidence: 0.7442109
00:12:47.545 --> 00:12:50.832 and up to it from Trimble that
NOTE Confidence: 0.7442109
00:12:50.832 --> 00:12:53.276 collaboration is basically something
NOTE Confidence: 0.7442109
00:12:53.276 --> 00:12:56.360 that is extremely important for us.
NOTE Confidence: 0.7442109
00:12:56.360 --> 00:12:59.570 And on the translational abside Stephanie
NOTE Confidence: 0.7442109
00:12:59.570 --> 00:13:03.165 for sure that has been instrumental in
NOTE Confidence: 0.7442109
00:13:03.165 --> 00:13:07.070 in the group as well as Manoj Pillai.
NOTE Confidence: 0.7442109
00:13:07.070 --> 00:13:10.838 Next slide, please.
NOTE Confidence: 0.7442109
00:13:10.840 --> 00:13:12.950 So as you may know,
NOTE Confidence: 0.7442109
00:13:12.950 --> 00:13:15.040 in MLP malignancy daughter asked
NOTE Confidence: 0.7442109
00:13:15.040 --> 00:13:17.967 basically 10 years we had a real
NOTE Confidence: 0.7442109
00:13:17.967 --> 00:13:21.559 paradigm shift thanks to the
NOTE Confidence: 0.7442109
NOTE Confidence: 0.7442109
00:13:24.340 --> 00:13:27.294 That’s been true in acute myeloid leukemia,
NOTE Confidence: 0.7442109
00:13:27.300 --> 00:13:28.988 so that’s really fast.
Through in the acute myeloid leukemia.

Then in my dysplastic syndrome, but is basically representative of what we have seen also in our knowledge of my wife, activities, orders, or bone marrow failures,

for example, and this revolution, in our understanding of the disease, translated more recently.

And we can switch style.

Um, in a boarding shift also in the management of this disease and since 2017 we add more approval than over the last 2025 years that goes with basically drug at R agnostic of any.
Potential genomic amenities such as the CP351 for example or more recently than 8:00 o’clock, but also drugs that are no standard of care for basically mutated diseases, such as flat 3 mutated AML or, potentially IDH mutated diseases. Interestingly, this revolution that started with the access my leukemia, we’re starting to see, speaking up. Also, in multiple packages, orders with the recent approval of Fedratinib as well as with my dysplastic syndrome with recently the approach the TGF beta inhibitor spider step
as well as the oral decision to be in. Stop all of that is extremely important and allow us to basically. Have a real improvement for or patient regarding prognostic forgetting option of treatment. But we still in situation where a cute smile, leukemias and melodies plastic syndromes are how to treat disease. If you standardize the incidence rate of looking at my leukemia, that’s still in the top five of the most deadliest cancer that we have to face in the US and one of the goals that we had.
In the group has been to really work at different aspect to try to improve the result of the different treatment and we can switch to the next slide. We really tried to work from single cell to population research and that’s just not basically to basically have a stun. But that’s really what is the MLP malignancy group going from. Stephanie was mentioning our first result in a single cell sequencing in acute myeloid leukemia.
As the researcher Stephanie Ann manner.

In the labs around uh. Mouse model of.

Testing syndromes RNA for montage

Testing syndromes RNA for montage to the collaboration that we have with the Cobra Group,

led by AMR Nikolai and Rory on outcome research.

From a pure clinical research, sense points or group has been instrumental in several key studies that led to approval of these drugs over the last few years, but or portfolio and our goal is really focused on early development of a new agent.

Right now click portfolio is
00:17:21.790 --> 00:17:26.568 roughly 40% of phase one trials.
NOTE Confidence: 0.8108151
00:17:26.570 --> 00:17:28.580 With.
NOTE Confidence: 0.8108151
00:17:28.580 --> 00:17:31.247 Basically a good #6 out of 19
NOTE Confidence: 0.8108151
00:17:31.247 --> 00:17:33.530 active trial that our investigator
NOTE Confidence: 0.8108151
00:17:33.530 --> 00:17:36.692 initiated trial and thanks to all
NOTE Confidence: 0.8108151
00:17:36.692 --> 00:17:39.618 the commitment of the research staff.
NOTE Confidence: 0.8108151
00:17:39.620 --> 00:17:42.626 Thanks to all of the commitment
NOTE Confidence: 0.8108151
00:17:42.626 --> 00:17:45.444 of the different members of Group
NOTE Confidence: 0.8108151
00:17:45.444 --> 00:17:48.308 we right now at a rate of index
NOTE Confidence: 0.8108151
00:17:48.402 --> 00:17:50.907 cases included in clinical trials
NOTE Confidence: 0.8108151
00:17:50.907 --> 00:17:55.301 on main campus that is 15 to 20%.
NOTE Confidence: 0.8108151
00:17:55.301 --> 00:17:57.809 Which is pretty remarkable.
NOTE Confidence: 0.83947045
00:17:57.810 --> 00:18:01.394 We definitely aim to do better and
NOTE Confidence: 0.83947045
00:18:01.394 --> 00:18:04.996 we definitely aim to be able to
NOTE Confidence: 0.83947045
00:18:04.996 --> 00:18:07.948 export the research we’re doing from
NOTE Confidence: 0.83947045
00:18:08.050 --> 00:18:11.122 the main campus to different side
00:18:11.122 --> 00:18:14.974 of the network and be able to add
00:18:14.974 --> 00:18:18.379 better access for our patients in the
00:18:18.379 --> 00:18:21.359 network as mentioned by Stephanie,
00:18:21.360 --> 00:18:25.469 we have pretty efficient and pretty large.
00:18:25.470 --> 00:18:27.892 Think annotate by bank and I think
00:18:27.892 --> 00:18:30.135 we can give kudos to Stephanie
00:18:30.135 --> 00:18:32.767 to each of the exports in 2011,
00:18:32.770 --> 00:18:35.690 so we’re in a decade in right now.
00:18:35.690 --> 00:18:37.880 We should definitely celebrate about that.
00:18:37.880 --> 00:18:40.800 And that gives us a lot of leverage,
00:18:40.800 --> 00:18:44.027 potentially to be able to develop some
00:18:44.027 --> 00:18:45.410 translation translational research.
00:18:45.410 --> 00:18:47.930 As well as potentially bringing
00:18:47.930 --> 00:18:50.450 some collaboration from the outside
00:18:50.529 --> 00:18:52.513 with pharmaceutical companies as
00:18:52.513 --> 00:18:54.704 we have pretty efficient and pretty large.
Just wanted to highlight basically two programs more than two studies to program. Basically going on the first one are the efforts led by armor side and on emerging approaches in my late malignancies and probably Anna does not remember, but I’ve even. Remember first discussion years ago when we were in Hopkins together when we were in Hopkins together. Around potentially all this knew, you know therapies can be instrumental in or disease disease type, basically. What has been done is basically around the additional,
uh, the 1st generation, but also right now the second generation of even the energy agent to conventional therapy. We're right now activating. Very broad induction chemotherapy plus volume up study under the umbrella of a sitter. With the first patient that we hope to include in the next few weeks, we just have finished the, uh, cool on the map plus entinostat NDS trial for the group of patients with mild agent Majestik syndrome
failed by accommodating agent, and we are looking forward for this data that has been basically possible to to develop thanks to. Elaboration with Yale Science and that’s work with initially TK came. One of us still here and we have also a chronic my leukemia studies sponsored by equal on the addition of bambrough on tyrosine kinase inhibitor for a patient with chronic migraine leukemias, an Axia Resul disease. Beside this trial, we also have been implicated. Basically thanks to our leadership on some of the development of the
newest generation of Elon College.

Agents such as the T in three inhibitor and we hope to have more results to show that in the near future next slide.

So the idea of the DS program? That’s something that I already presented basically a few weeks ago during the ground rounds, but I definitely like this program as it’s really a homegrown program thanks to the work and interaction with Stephanie and Ranjit.

So that’s really a good example of what we can achieve at yelling working together.

We have been able to show how
we can exploit the weaknesses of IDH mutated AML in NDS.

As you can see.

When we have an idea of mutation and the presence of two HG in the media that creates some braknis phenotype that can be potentially targeted by using popped inhibitor on the upper right side. Can see that treatment with olaparib in a primary samples in grafted in mice can potentially significantly reduced the disease burden in. Lisa grafted with acute myeloid leukemia.
the resistance to IDH inhibitors in the clinic and that led to the step trial.

Brentley ongoing with right now.

Six patient included,

including four at.

At here with basically the use

of elaborate the parking meter.

For a male and MBS patient with IDH mutation.

Interestingly,

for the discussion with the tap,

we've been able to have a patient that

were not yet exposed to IDH limit,

or potentially integrating the trial

with an early evaluation that would also

potentially to switch to ID age limit,
or there was no some clearcut benefit

That’s two of the main program

That we have right now.

I’m not going to basically talk

too much about the outcome.

Research as we add with basically.

Nicole,

I would review of what was going on

on this Group A few a few weeks ago,

but as we were discussing we really

want to be able to to bridge the

most basic science aspect of it.

What we’re doing in the in the labs

to this outcome. Research go go ahead.

We still have a lot of people
00:24:19.992 --> 00:24:22.160 in the results clinical issue.

00:24:22.160 --> 00:24:23.628 Then that’s the topic.

00:24:23.628 --> 00:24:26.240 We’re not the addressing all of them,

00:24:26.240 --> 00:24:28.406 but some of them are definitely

00:24:28.406 --> 00:24:30.699 on the focus of the group.

00:24:30.700 --> 00:24:32.722 The management of high risk disease

00:24:32.722 --> 00:24:35.520 in AML and MD S complex karyotype.

00:24:35.520 --> 00:24:38.033 NLL mutated or rearrange disease are one

00:24:38.033 --> 00:24:41.076 of the focus of development of the group.

00:24:41.080 --> 00:24:44.044 And I specially Rory is developing

00:24:44.044 --> 00:24:46.020 some different concepts around.

00:24:46.020 --> 00:24:46.772 These lines,

00:24:46.772 --> 00:24:48.276 the optimization of targeted

00:24:48.276 --> 00:24:49.780 therapies and email steropes.

00:24:49.780 --> 00:24:52.788 We talked about that one of the challenges,
basically that we’re still working with the disease that is not as common as breast or colon cancer, and we end up with more combination and sequence of agent then patient. And that’s potentially where the interaction with the lab and the work that we’re doing with Stephanie is extreme and mineral. Extremely important. Targeting of leukemia stem cell looking initiating cells and management. Measurable residual disease at the molecular level is obviously something that is on our mind, and that’s a lot of interaction.
Also with the transplant group in South Therapy Group on our potentially to work around this concept.

And last but not least, before getting to the point where we have active disease, working on predisposition and potentially climb.

This is something that is extremely interesting right now with. In collaboration we will have.

With the cardiology group and the Generation project,
Feel that we were pretty blessed in the group to have already's. Pretty solid foundation, but we wanted to do better and that's gonna be by leveraging the excellence that we have it here the molecular biology aspect with basically right now are some development in single cell sequencing using multi omics approaches that can potentially be used in my life but not only in my right mind agencies. Potential collaboration and avenues of collaboration with the yellow. Center of immuno oncology. And with a group of Marcus mention also to potentially work on resistance disease,
immuno oncology in my redemer agencies

and the really fruitful and really exciting collaboration we have with the Copper Group carry gross schalmei.

With a lot of publication and lots more that will come in the next. We want to expand our collaboration. That’s going to be more collaboration and more on the stage with us in more portable computers as well as more collaboration on the clinical research side.
Obviously with the BMT and cell Therapy Group, but also without regard for the adolescent young adults, and I think that’s all I have. Thank you so much tomorrow. This is really awesome, so we’ll go straight into our next presentation by Doctor Falls on behalf of Mylan Malignancy’s team. Hi, this is Francine and I’d like to thank Stephanie and also Charlie for all of your work to bring us to where we are today with this faculty on the development of your work to bring us to where we are today with this faculty on the development of Mylan Malignancy.”
00:28:04.010 --> 00:28:05.738 Scott Huntington, ERISA, Soupy,

00:28:05.738 --> 00:28:07.463 Shalin, Kothari, Toshin Sethi,

00:28:07.463 --> 00:28:08.756 an Francesco Montanari,

00:28:08.760 --> 00:28:11.784 both of whom have recently joined us.

00:28:11.790 --> 00:28:15.122 Francesca is in Greenwich.

00:28:17.296 --> 00:28:20.838 So this is the landscape of lymphoma.

00:28:20.840 --> 00:28:23.000 So lymphoma really is many different

00:28:23.000 --> 00:28:24.885 diseases, and that’s a challenge for

00:28:24.885 --> 00:28:27.699 us as a group with limited resources.

00:28:27.700 --> 00:28:30.220 Terms of trying to figure out how

00:28:30.220 --> 00:28:32.318 we focus this clinical trial effort.

00:28:32.318 --> 00:28:35.502 So it turns out that out of the 21,000

00:28:35.502 --> 00:28:38.169 cases of cancer in Connecticut per year,

00:28:38.170 --> 00:28:40.277 there are about 900 plus or minus
cases of non Hodgkin’s lymphoma.

So that’s really our denominator

population in our efforts are to

try to get many of these patients.

Want to clinical trials?

If you look at the curve at the

bottom you can see the frequency of

the different types of non Hodgkin’s

lymphoma with diffuse large B cell lymphoma,

follicular lymphoma,

the low grade marginal zone lymphoma

is being the most common subtypes,

and T cell,

lymphoma and mantle and mantle

cell lymphoma and burqas are.

You can see are rare compared
to these other common subtypes.

Next slide.

Um, so the unresolved political issues, of course, are how we make sense of 90 different subtypes of lymphoma and divide those into general themes.

For clinical trials, I'll talk a little bit about that in a minute, but you know, we do have diseases where the modern regimes pretty much are OK in terms of producing favorable outcomes for these patients.
but there are within these more favorable subgroups of patients.

Those patients with high risk molecular features that continue to fail conventional therapy and would be subjects for novel clinical trials and those include double hit diffuse, large B cell lymphoma and one of the things that we.

Done with that disease is to combine dose adjusted epoch with Lenalidomide. In addition, we have some patients with low risk lymphoma where we could actually test D escalation of therapy and a good example of that is classical...
Hodgkin's disease and I'm going to show you another example. For diffuse large B cell lymphoma we also have histologies where the modern regimens are ineffective, pretty much inadequate for these aggressive patients such as the T cell lymphoma's. The piece of distributing mantle cell lymphoma's and the post transplant lymphoproliferative disorders so in these cases where are trying to incorporate novel agents into the frontline but also trying to figure out how to incorporate.
allogeneic stem cell transplant and the newer car T cell therapies, would love to use molecular and genetic profiling in these diseases to select patients rationally for pathway directed clinical trials, and those efforts are now underway thanks to the work of Stephanie. To get our tissue bank up and running. Sorry sorry, OK next slide. So, um, just touching on how we’re deescalating therapy. This is a really great example of a trial that Scott has opened for relapsed aggressive B cell lymphoma’s where we have a non chemotherapy approach.
So basically this study involves oral agents of BTK inhibitor and mtor inhibitor, an image, and it turns out that when you combine these three oral therapies, this is a very effective strategy for patients with aggressive lymphoma who have failed conventional chemotherapy. Some of them have failed transplant as well. On the next slide, Stephanie, you can see an example of one of our patients. It turns out that yall actually has involved the majority of patients that were 21 patients to date in this trial and responses have been observed among.
a different subtype of patients.

You can see with DL, BCL with low grade lymphoma, mantle cell lymphoma etc and patients with very dramatic responses with large masses and extensive disease. So we were really excited about this approach. And again, we'd all like to start thinking more about oral rather than Ivy therapies for patients that are going to be chronically needing therapy, such as many of our lymphoma patients. Unfortunately, next slide would highlight another approach,
which is to take an active drug, look at its resistance mechanisms and come up with. Similar drugs that might be active in resistant mutational settings. In this case, BTK inhibitors are one of our most active newer agents in B cell lymphoma, but most of the failures to these agents are related to the development of specific mutations and now we have these new non covalent BTK inhibitors that actually are able to subvert those mutations and induced responses in patients and this is an
agent that we're working with now.

Locks 0305.

Falls into that category that's highly active.

We are currently embarking upon a number of phase two studies that we hope to make available broadly across our care centers looking at a number of different B cell lymphoma is with these novel agents.

So Charlyn is looking at ways of translational research done by shelling pathari in our group.

So Charlyn is looking at ways of.
Dealing with the development of resistance to active agents such as phonetic, LAX, and hear a set of experiments where he has shown that proteasome inhibition is synergistic with phonetic lacks in patients with B cell lymphoma an. In these clinical models, so you can see the bot is mid carve. Is Mebane exacerbated by themselves, which are proteasome inhibitors have some activity to induce a pop ptosis? As does phonetic LAX? But when you combine these agents you can see synergistic activity.
And based on this in vitro work that Charlene has done, he’s embarking on a seat app sponsored Phase 1, two clinical trial where he’s combining genetic LAX with these proteasome inhibitors and we’re very excited for Shaolin to get that trial up and running on the next slide, you can see the correlative science that’s developed around this clinical trial, including a single celled Association to look at these specific BCL, two family members. By Aqua, as well as by mass spec. He’s also doing exome sequencing,
NOTE Confidence: 0.8098004
00:34:39.390 --> 00:34:42.438 RNA seek and trying to obtain tissues from
NOTE Confidence: 0.8098004
00:34:42.438 --> 00:34:45.010 these patients for later PDX development.
NOTE Confidence: 0.8098004
00:34:45.010 --> 00:34:47.691 So that’s all very exciting and we’re
NOTE Confidence: 0.8098004
00:34:47.691 --> 00:34:50.220 really proud of shelling for that.
NOTE Confidence: 0.8098004
00:34:50.220 --> 00:34:53.062 In additional, he’s he’s doing what other
NOTE Confidence: 0.8098004
00:34:53.062 --> 00:34:56.135 groups are doing to embark on looking for
NOTE Confidence: 0.8098004
00:34:56.135 --> 00:34:59.040 a circulating tumor DNA in these patients,
NOTE Confidence: 0.8098004
00:34:59.040 --> 00:35:02.050 and hopefully some of us will be
NOTE Confidence: 0.8098004
00:35:02.050 --> 00:35:04.580 able to incorporate that into our.
NOTE Confidence: 0.8098004
00:35:04.580 --> 00:35:09.428 A disease group studies as well next slide.
NOTE Confidence: 0.8098004
00:35:09.430 --> 00:35:11.926 So and then the last thing I want
NOTE Confidence: 0.8098004
00:35:11.926 --> 00:35:14.128 to mention is exciting work that
NOTE Confidence: 0.8098004
00:35:14.128 --> 00:35:16.840 Charlene is doing with the Cats lab
NOTE Confidence: 0.8098004
00:35:16.840 --> 00:35:19.138 to use a different approach called
NOTE Confidence: 0.8098004
00:35:19.138 --> 00:35:21.014 protest back to target antiapoptotic
NOTE Confidence: 0.8098004
proteins potentially, but their critic benefit soap Protex basically is a hetero bifunctional small molecule that consists of a linker and two warheads. One of them binding to the target protein such as the BCL two and the other recruiting the E3 ligase to basically leads to the degradation of that. Protein, so we're looking forward to this work coming to fruition in the clinic in the future. Just highlights some of the work that Scott has done working with the Copper Group to look at
outcomes in patients with lymphoma. And so Scott has done a number of studies including these two, one of which shows that patients with who are older than 80 have a higher frequency of discontinuing active therapies like a brute, not within the first 180 days. So obviously one has to go back and look at why that is and ways that we can. Alter that therapy so those patients can continue to be treated and then also Scott has done a lot of work with cost effectiveness and this is just one of his studies looking
00:36:29.630 --> 00:36:31.230 at different treatments for CLL.
NOTE Confidence: 0.8098004
00:36:31.230 --> 00:36:32.830 Getting a brute nip upfront
NOTE Confidence: 0.8098004
00:36:32.830 --> 00:36:34.430 versus getting it later on.
NOTE Confidence: 0.8098004
00:36:34.430 --> 00:36:34.998 So again,
NOTE Confidence: 0.8098004
00:36:34.998 --> 00:36:36.702 Scott has presented some of this
NOTE Confidence: 0.8098004
00:36:36.702 --> 00:36:38.590 work at the national meetings.
NOTE Confidence: 0.8098004
00:36:38.590 --> 00:36:41.128 Then there are a number of
NOTE Confidence: 0.8098004
00:36:41.128 --> 00:36:42.820 studies ongoing with copper.
NOTE Confidence: 0.8098004
00:36:42.820 --> 00:36:46.303 Next slide will then segue us into T cell.
NOTE Confidence: 0.8098004
00:36:46.310 --> 00:36:48.250 Lymphoma is T cell lymphoma.
NOTE Confidence: 0.8098004
00:36:48.250 --> 00:36:50.175 Is overall are heterogeneous as
NOTE Confidence: 0.8098004
00:36:50.175 --> 00:36:53.228 arvis bonas and tend not to do as
NOTE Confidence: 0.8098004
00:36:53.228 --> 00:36:54.983 well with conventional therapies as
NOTE Confidence: 0.8098004
00:36:54.983 --> 00:36:57.822 you can see in the outcomes curve
NOTE Confidence: 0.8098004
00:36:57.822 --> 00:36:59.882 progression free survival in median
NOTE Confidence: 0.8098004
00:36:59.890 --> 00:37:02.606 survival is poor for many of these.
Aggressive T cell subtypes.

The next slide.

Highlights one of the things that we’ve been trying to do so patients with T cell lymphoma get chop based chemotherapy upfront and only a small percentage of them actually are cured.

With this approach, patients would go on to an autologous stem cell transplant if they have a complete remission, but it turns out that when you look at registry studies, one of which we conducted here, only about 25% of patients
00:37:31.135 --> 00:37:32.800 upfront ever make a transplant.
NOTE Confidence: 0.8620923
00:37:32.800 --> 00:37:35.502 The reason being that many of those
NOTE Confidence: 0.8620923
00:37:35.502 --> 00:37:37.929 patients don’t have a good remission.
NOTE Confidence: 0.8620923
00:37:37.930 --> 00:37:40.495 And so this is a study that I worked
NOTE Confidence: 0.8620923
00:37:40.495 --> 00:37:43.095 on with tar Sheen and this study
NOTE Confidence: 0.8620923
00:37:43.095 --> 00:37:45.480 is hopefully going to get started
NOTE Confidence: 0.8620923
00:37:45.480 --> 00:37:47.934 very soon where we combined Mogamu
NOTE Confidence: 0.8620923
00:37:47.934 --> 00:37:49.843 Lizum app with upfront chemotherapy.
NOTE Confidence: 0.8620923
00:37:49.843 --> 00:37:52.010 In this case, epoch for patients
NOTE Confidence: 0.8620923
00:37:52.010 --> 00:37:53.810 with aggressive T cell lymphoma.
NOTE Confidence: 0.8620923
00:37:53.810 --> 00:37:55.940 The idea being that Mogamulizumab is
NOTE Confidence: 0.8620923
00:37:55.940 --> 00:37:58.102 a CCR four monoclonal antibody that
NOTE Confidence: 0.8620923
00:37:58.102 --> 00:38:00.798 targets both tumor cells at but also more
NOTE Confidence: 0.8620923
00:38:00.862 --> 00:38:03.557 importantly T regs in the micro environment,
NOTE Confidence: 0.8620923
00:38:03.560 --> 00:38:05.540 so we’re hoping that there’s
NOTE Confidence: 0.8620923
00:38:05.540 --> 00:38:07.520 going to be an interaction.
Both in the micro environment as well as potential synergy with the tumor cells. When this is combined with chemotherapy, I don’t have a slide to show you this, but, uh, she has also developed some very nice correlative studies to go along with this. The next slide.

Will take you into the world of relapsed T cell lymphoma and just to demonstrate to you the work of our group to look at a number of different agents targeting a number of different pathways that are relevant and some of these studies. Yale has been the top one or two in terms of accrual for these studies.
nationwide and these are novel agents and I'll touch on a couple of them in the next slide or two.

Um, go back and this is next slide. OK, this is tipifarnib which is a farnesyltransferase inhibitor, but it turns out that it also down regulates CX CL 12 which is in the micro environment patients who have expression of CX CL 12 in the micro environment don’t do as well as you can see on this survival curve and we’ve had some incredibly dramatic responses using this single oral agent and some of our patients
such as this gentleman who has failed multiple therapies in autologous transplant that this is really salvage. A lot of people were hoping to initiate some Iits with this molecule in the next couple of months. Next slide shows you another approach with micro RNA, so this is the first in man study of this micro RNA which targets a number of different types of lymphoma. We put a number of patients with cutaneous lymphoma on this trial and you could see responses in pretty much all of the patients that were treated.
Based on these waterfall plots and on the next slide I think is really one of the most important findings. This micro RNA, which is its activity in HTLV one associated adult T cell leukemia, and again we put the majority of patients in this cohort on this trial and we also initiated the correlative studies that you see below, showing that the molecule directly inhibits the proliferation of ATL cells. Modulates the expression of various activation markers and you can see the changes in proliferation index with this molecule and this is.
All samples from our patients that were drawn at different time points, so we’re very excited to get this data published.

Next slide. Just a couple of other studies initiated. This is another of Pershing study looking at incorporation of pembrolizumab with an active agent Brentuximab dowtin in CD 30 positive T cell lymphoma is and again this is her IIT and there are some correlative studies associated with this and the next slide.

Yeah, the next slide will segue into.
some of the efforts that Francesca has looking at in a couple of different areas. In the context of aggressive lymphomas, this is her global T cell consortium study, which she conducted at Columbia and is now brought to Yale, and this is now a randomized phase two study where she’s looking at 5:00 or oral is incited gene in Rome and Epson compared to investigators choice. This is a multicenter study. And we’re really excited that Francesca has brought this to us and the next slide is another effort in an area that we have not explored. Which is PTLD so post transplant
lymphoproliferative disorders.
In this study, Francesca is using sequential treatment for patients that are CD 20 and CD 30 positive and you can see the scheme for this trial here. This is also an IIT that’s being conducted in collaboration with the Mayo Clinic. Would you be a? So I think we have some really nice work from some of our younger investigators and we’re very excited about that.

The next slide. Is just our summary slide looking at what our future is and where we’re hoping.
to go in the lymphoid malignancy’s.

So clearly we will benefit from the annotated database that you’ve heard about and hopefully will be contributing our samples in an ongoing fashion to the biobank.

We also need to develop a sequencing platform which we really don’t have here at the institution.

For lymphoma we’re currently sending our samples out, but we certainly would like to do that in the near future.

I talked about the biobank and how important that is, but also we’re now starting to talk about
00:42:51.454 --> 00:42:53.069 thematic direction for the program, 

00:42:53.070 --> 00:42:55.275 and one of the areas that we’re 

00:42:55.275 --> 00:42:57.998 focusing on at least in T cell lymphoma, 

00:42:58.000 --> 00:42:58.984 as you’ve seen, 

00:42:58.984 --> 00:43:00.624 is on the micro environment, 

00:43:00.630 --> 00:43:02.185 and you know immunomodulatory strategies 

00:43:02.185 --> 00:43:04.486 that can be used with correlative science 

00:43:04.486 --> 00:43:06.556 in these two cell lymphoma studies, 

00:43:06.560 --> 00:43:07.586 and then finally, 

00:43:07.586 --> 00:43:09.638 I just want to acknowledge the 

00:43:09.638 --> 00:43:10.686 translational science collaborators 

00:43:10.686 --> 00:43:12.961 and this by no means is an 

00:43:12.961 --> 00:43:14.118 exhaustive list of folks, 

00:43:14.120 --> 00:43:16.500 but there have been a number of. 

00:43:16.500 --> 00:43:19.260 Studies that have been funded by both DeLuca 

NOTE Confidence: 0.8136023
as well as other mechanisms for funding, and those include studies done with the Cats lab with Marcus is lab, which is now being engaged with these studies. The Lola slab in pharmacology and even the imaging labs with a nuclear medicine with Doctor Chi and others that I didn’t mention as well. So I think we have a very bright future ahead of us in the lymphoid malignancies. Thank you, Stephanie. Thank you for I’ve jumped.
00:43:53.816 --> 00:43:55.808 is so excited about everything that
00:43:55.872 --> 00:43:58.112 is to come and very excited about
00:43:58.112 --> 00:43:59.710 our next presentation by Doctor
00:44:01.600 --> 00:44:01.600 Natalia never eats a on multiple
00:44:01.600 --> 00:44:02.617 myeloma in commodities.
00:44:02.617 --> 00:44:04.990 Stephanie, thank you so much for the
00:44:05.052 --> 00:44:06.816 opportunity to let me present today
00:44:06.816 --> 00:44:09.546 and I would like to echo some of your
00:44:11.680 --> 00:44:11.680 comments and thank thank Charlie for his
00:44:13.570 --> 00:44:13.570 outstanding leadership at the Cancer Center.
00:44:15.495 --> 00:44:15.495 So today I’m happy to present on
00:44:17.469 --> 00:44:17.469 behalf of myeloma team with brief
00:44:18.917 --> 00:44:18.917 clinical and research updates.
00:44:20.810 --> 00:44:20.810 Here’s our team myself. Terry Parker.
00:44:22.470 --> 00:44:22.470 Know far Bar and Sabrina.
Browning as well as Elon Gorshin at Guilford.

I'll start with brief Brecht background about the disease. As you all know, multiple myeloma is the clonal plasma cell neoplasm originating in the bone marrow. The diagnosis rests on the bone marrow biopsy and some of the key immunohistochemical stains and protein studies on the blood in the urine. The ETL pathogenesis of this disorder remains largely obscure. We know of certain associations, such as perhaps antigenic stimulation. Role of.
Pathogenic microbes, lipid antigens and other associations such as metabolic syndromes, diabetes and such, but in large majority of patients we don’t know the cause and much remains to be elucidated in this research.

So as you know, the diseases continuum and we know that myeloma every case is preceded by the precursor state called M Gus monoclonal gammopathy of undetermined significance and after years of its presence it progress.
is to the early phase myeloma, commonly referred to as small during or asymptomatic myeloma. But a full blown clinical disease which requires active therapy is the disease which leads to end organ damage in the form of high calcium, renal failure, anemia and bone lesions. And in the old days we would resort to plane X Rays. However, this has been largely replaced by advanced imaging modalities such as whole body MRI or Whole Body PET CT scans. So once diagnosed,
the treatment pattern of multiple myeloma consists of initial induction therapy with usual 3 drug, or in 2021 you might choose a four drug regimen incorporating some of the monoclonal antibodies upfront, such as daratumumab in appropriate patients. This is then followed by high dose melphalan, an autologous stem cell rescue AKA auto transplant, and then this is subsequently followed by maintenance therapy, which is usually long term and mental progression of disease. So the.
Treatment pattern resembles a marathon rather than the Sprint. As we continue maintenance for many years, for those patients who remain in remission next. And invariably, sooner or later, every patient experiences their relapse, and this is due to branching pattern of clonal evolution or push persistence of previous clones and at the time of relapse patients have to sequence through the available therapies, each of which then leads to shorter and shorter overall duration of response, eventually leading to dismal prognosis for many of their refractory patients.
Next please. Fortunately, we’ve had number of drug approvals over the course of the past decade, which includes the novel proteasome inhibitors in the form of carfilzomib as well as checkpoint inhibitor, targeting SLAM F7 or CS1, and others. The biggest breakthroughs came in 2015, when we had several approvals, namely IgG monoclonal antibody targeting CD38 receptor on the plasma cell daratumumab, as well as checkpoint inhibitor, targeting SLAM F7 or CS1, and others. Orally available Proteus inhibitor.
We also had approval for histone deacetylase inhibitor PANOBINOSTAT which is orally available and more recently a drugs of completely different mechanism affection such as selinexor received approval by FDA in 2019. This is a selective nuclear export inhibitor promoting some of the tumor suppressor gene action and within the past year approval of another IgG monoclonal antibody. Against CD 38 is I took some up with slightly different mechanism of action, but very similar to daratumumab and more recently just summer of last year. First antibody drug conjugate

00:48:21.230 --> 00:48:23.534 This is Bill on time Out method Odin targeting B cell maturation antigen which is currently approved for relapsed refractory multiple myeloma.

00:48:23.534 --> 00:48:25.530 targeting B cell maturation antigen

00:48:25.530 --> 00:48:27.785 which is currently approved for relapsed refractory multiple myeloma.

00:48:27.785 --> 00:48:29.770 Beyond four prior lines of therapy next.

00:48:29.770 --> 00:48:34.439 So despite these therapeutic advances, number of clinical challenges remain primarily the concerns about what to do for refractory myeloma.

00:48:34.440 --> 00:48:36.350 So despite these therapeutic advances, number of clinical challenges remain primarily the concerns about what to do for refractory myeloma.

00:48:36.350 --> 00:48:37.954 Are we able to, in the novel immunotherapy era, replaced the high dose melphalan by some of the novel strategies such as car T cell or other therapeutics?

00:48:37.959 --> 00:48:42.078 what to do for refractory myeloma.

00:48:42.080 --> 00:48:43.608 Are we able to, in the novel immunotherapy era, replaced the high dose melphalan by some of the novel strategies such as car T cell or other therapeutics?
00:48:52.780 --> 00:48:55.138 How best to continue the maintenance
NOTE Confidence: 0.8280961
00:48:55.138 --> 00:48:56.710 therapy for patients particularly
NOTE Confidence: 0.8280961
00:48:56.769 --> 00:48:58.509 high risk data genetic subsets?
NOTE Confidence: 0.8280961
00:48:58.510 --> 00:49:00.880 And we’re far from understanding the
NOTE Confidence: 0.8280961
00:49:00.880 --> 00:49:02.882 disease biology and choosing this
NOTE Confidence: 0.8280961
00:49:02.882 --> 00:49:05.030 sequential therapy based on biology of
NOTE Confidence: 0.8280961
00:49:05.030 --> 00:49:07.448 disease and its selection of therapy.
NOTE Confidence: 0.8280961
00:49:07.450 --> 00:49:09.774 Any cases is random and this is
NOTE Confidence: 0.8280961
00:49:09.774 --> 00:49:10.770 a clinical challenge.
NOTE Confidence: 0.8280961
00:49:10.770 --> 00:49:12.756 Same is true for a llama.
NOTE Confidence: 0.8280961
00:49:12.760 --> 00:49:13.424 Lodosa is,
NOTE Confidence: 0.8280961
00:49:13.424 --> 00:49:14.420 as you know,
NOTE Confidence: 0.8280961
00:49:14.420 --> 00:49:16.150 about 10% of multiple myeloma
NOTE Confidence: 0.8280961
00:49:16.150 --> 00:49:17.534 patients will develop concurrent
NOTE Confidence: 0.8280961
00:49:17.534 --> 00:49:19.487 soft tissue deposition of the Lambda
NOTE Confidence: 0.8280961
00:49:19.487 --> 00:49:20.727 or Kappa light chains,
and this is an unmet need in all of the gammopathy world as these patients, the care is not well defined, so it remains to be established what is the optimal first line, second line and beyond therapy for patients with this next please. So while facing these challenging issues in clinic we tried to integrate our clinical expertise and incorporate some of the Noble research therapeutic strategies and continue to educate our patients as well as our trainees next. In terms of individual focus of
clinical expertise, Terry Parker has an outstanding clinical expertise in a llama low doses having served as National Pi and number of a alloy doses, trials as well as relapsed refractory myeloma. Nofar nofar sparkles has been mostly on high dose melphalan. Autologous stem cell transplant for myeloma as well as cellular therapies in myeloma. Sabrina also has an excellent expertise in a llama low doses shoot the separate fellowship in amyloidosis at the Boston Medical Center. She also focuses on understanding the biology of some of the
00:50:28.748 --> 00:50:30.658 precursor States and my own.

00:50:30.660 --> 00:50:33.205 Clinical research has focused on's

00:50:33.205 --> 00:50:35.241 to understanding clonal heterogeneity

00:50:35.241 --> 00:50:38.164 and incorporating advanced imaging in

00:50:38.164 --> 00:50:40.508 this disease therapeutic assessment.

00:50:40.510 --> 00:50:43.107 So education is of course an integral

00:50:43.107 --> 00:50:45.049 component of our daily work.

00:50:45.050 --> 00:50:47.535 This is a group of current fellows

00:50:47.535 --> 00:50:49.079 rotating through myeloma clinics

00:50:49.079 --> 00:50:50.719 during this academic year,

00:50:50.720 --> 00:50:53.331 and many of them have been involved

00:50:53.331 --> 00:50:55.249 in research projects in myeloma.

00:50:55.250 --> 00:50:56.294 So, for instance,

00:50:56.294 --> 00:50:58.382 Weixin Lou has been working on

00:50:58.382 --> 00:51:00.168 myeloma Yale Database project.

00:51:00.320 --> 00:51:02.189 One thing that we're working on

00:51:02.191 --> 00:51:04.482 is using these imaging techniques

00:51:04.484 --> 00:51:06.986 to look at the evolution of disease.

00:51:06.988 --> 00:51:09.938 So in the early stages,

00:51:09.940 --> 00:51:12.338 we see a lot of heterogeneity

00:51:12.340 --> 00:51:14.658 in the disease.

00:51:14.660 --> 00:51:16.738 As we follow these patients,

00:51:16.740 --> 00:51:19.285 we see that over time,

00:51:19.287 --> 00:51:21.785 the disease becomes more homogeneous.

00:51:21.787 --> 00:51:24.015 So we're able to track the progression

00:51:24.074 --> 00:51:26.627 of the disease.

00:51:26.630 --> 00:51:29.108 This is really important for therapeutic assessment.
On looking at outcomes in patients treated with monoclonal antibodies, Talib Dasani has the bone disease in myeloma cohort and looking to develop quality improvement project started. Targeting this Eric Chang will be involved in this promise study, which is the screening and community outreach project for patients with gammopathy’s and their families, and it has an important outreach project, and we’re partnering with Dana Farber Doctor Ghobrial on this project. And finally, Rose Mirkin will be involved in the collaborative effort where we
may study the antigenic targets of monoclonal antibodies of myeloma with the help of immunology. Lab of.

So our research consists of different missions. On one hand, we always try to enhance our clinical trial portfolio. We have ongoing trials, both investigator initiated as well as industry and collaborative group trials. In every space of this disease, including early stage, small during as well as newly diagnosed and late relapsed refractory patients.
And we always try to develop additional therapeutic concepts for refractory myeloma.

Andale Emily doses.

On the other hand, we do have certain outcomes, research initiatives and this include both myeloma as well as Mgas database as well as bone disease.

In myeloma collaboration with our copper team and finally on the research basic Science Research front, we've been trying to build teams to collaborate with researchers.

They're driving antigens and Additionally mean profiling to understand predictive
biomarkers of disease response.

And study extramedullary disease next please.

So on the basic science research front,

I think the.

Stephanie Collins, Biobank project for hematology has been really instrumental in our program at North Haven Myeloma program.

We've essentially biobank the bone marrow and peripheral blood on every single patient that we diagnosed with multiple myeloma or gammopathy, and we hope to build collaboration and with the help from David Shatz lab to develop ex vivo multiple myeloma.
00:53:18.272 --> 00:53:21.122 mouse models where we can develop
NOTE Confidence: 0.8216927
00:53:21.122 --> 00:53:23.573 robust preclinical models using this.
NOTE Confidence: 0.8216927
00:53:23.573 --> 00:53:24.659 In addition,
NOTE Confidence: 0.8216927
00:53:24.659 --> 00:53:26.288 studying monoclonal antibodies
NOTE Confidence: 0.8216927
00:53:26.288 --> 00:53:28.460 and understanding the antigenic
NOTE Confidence: 0.8216927
00:53:28.528 --> 00:53:31.060 targets and what drives the disease
NOTE Confidence: 0.8216927
00:53:31.060 --> 00:53:33.232 in collaboration with Aaron Rings
NOTE Confidence: 0.8216927
00:53:33.232 --> 00:53:35.297 lab on clinical research front,
NOTE Confidence: 0.8216927
00:53:35.300 --> 00:53:37.808 we’ve had active clinical
NOTE Confidence: 0.8216927
00:53:37.808 --> 00:53:40.943 collaboration and couple of IIT’s.
NOTE Confidence: 0.8216927
00:53:40.950 --> 00:53:42.666 Closely working with musculoskeletal
NOTE Confidence: 0.8216927
00:53:42.666 --> 00:53:44.811 radiology and in this and
NOTE Confidence: 0.8216927
00:53:44.811 --> 00:53:46.229 haimson ending lishouk,
NOTE Confidence: 0.8216927
00:53:46.230 --> 00:53:48.430 both have been instrumental as
NOTE Confidence: 0.8216927
00:53:48.430 --> 00:53:50.630 well as our pathology colleagues.
NOTE Confidence: 0.8216927
00:53:50.630 --> 00:53:53.710 Mean issue and sang and pen know.
Farhan Sabrina have ongoing collaboration with an Habermann from lab laboratory medicine to understand immune profiling of patients to understand the biologic response in different subsets of myeloma patients treated with monoclonal antibodies in terms of outcomes research. We’ve had active collaboration with the leadership of Shammai, my and Scott Huntington, we have several ongoing projects, and one of them a recent one using flat iron database and one particular
myeloma project examining patterns of care, especially in the context of kovid period. And Lastly, we've been trying to build this disease team, which we refer to myeloma bone disease program collaboration, under which we try to bring together different departments, including Endocrinology, Carlin, Sonia, as well as orthopedic and spine center, Dieter, Lindskog, and Louise called. And as I said, Talib Dosani has an ongoing outcomes project looking into bone disease in myeloma. So with that I will stop. I’m exciting to have such great
collaborators and colleagues on the campus. And I will leave a couple of minutes for questions. Thank you so much. Awesome, alright, so I’ll share my screen. Just people know we have hematology joins 2021. We have a Twitter handle so we’ll try and use it, so I’m going to unshare so we can see everybody and let me pull up the chat to see if there are questions. Are there questions? Would anybody like to raise their
hand and ask the question? 
NOTE Confidence: 0.8470994

If not, I can start with one and then 
NOTE Confidence: 0.8470994

maybe I’ll ask Francine since I’m 
NOTE Confidence: 0.8470994

always a molecular person and I know 
NOTE Confidence: 0.8470994

that we have this phenomenal effort 
NOTE Confidence: 0.8470994

to get on this goal panel and whole 
NOTE Confidence: 0.8470994

exome sequencing tower patients. 
NOTE Confidence: 0.8470994

Do you think that that will 
NOTE Confidence: 0.8470994

fulfill your need? 
NOTE Confidence: 0.8470994

Or what do we need to do to improve on that? 
NOTE Confidence: 0.886944

I think that’s certainly a start. 
NOTE Confidence: 0.886944

You know, as you know Stephanie, 
NOTE Confidence: 0.886944

we see some of these. 
NOTE Confidence: 0.886944

We are rare lymphoma patients for whom 
NOTE Confidence: 0.886944

there’s really no treatment algorithm 
NOTE Confidence: 0.886944

and which is kind of picking out of
a hat to try to figure out what to do
in the error of precision medicine.
I really think that we should be profiling
these patients and sequencing them
and rationally developing strategies,
so we would love to be able
to start doing that.
I think the critical component of that is,
you know, is being able to get hold
of that issue when it’s biopsied,
and to get it to the right place
as soon as possible.
We’re also very interested in
looking at circulating tumor cells
and whether that’s a strategy that
we could use as well.

OK

fantastic exciting.

Are there any other questions?

I don’t see any in the chat.

So one of the friends, you know, I guess I would ask and I think you each allude to it, but where do you think cell therapy is going?

And obviously it’s relevant to each of the domains being described.

So where do you think five years from now will be with respect to cell therapies?

Well, we talk a lot about that with respect to transplant that we were just
00:57:19.299 --> 00:57:21.177 talking out at BMT rounds today.

00:57:21.180 --> 00:57:23.178 About whether we’ll be doing autologous

00:57:23.178 --> 00:57:24.930 transplants in the future or not.

00:57:24.930 --> 00:57:26.835 I think that that’s kind

00:57:26.835 --> 00:57:28.359 of where we’re heading.

00:57:28.360 --> 00:57:30.320 I just wanted to say that one of

00:57:30.320 --> 00:57:31.958 the things that yell is doing,

00:57:31.960 --> 00:57:33.738 by the way, is we are developing

00:57:33.738 --> 00:57:35.574 our own party and we didn’t get

00:57:35.574 --> 00:57:37.098 a chance to talk about that.

00:57:38.355 --> 00:57:39.920 have developed the RNA car strategy

00:57:39.920 --> 00:57:41.205 and we’re working on that.

00:57:41.210 --> 00:57:42.978 I know he has a B cell construct

00:57:42.978 --> 00:57:44.809 as well as one vertice Oklahoma,
so I think the whole car world is undergoing evolution as well. And hopefully we’re going to be at the forefront of some of that. Don’t there’s a question from the audience will then from Doctor Chi with a new drug substitute of chemotherapy. In treatments. Also, with the new drug substitute chemotherapy treatment. From Doctor Chi. Yeah, I mean, I think that’s a question to everybody. Can we get rid of chemo? This toxic stuff? We are that we added Temple where we were able to do that,
like I acute firestick leukemias.
I mean, that’s a poster child, I know.
But potentially yes, that can be.
That can be the one of the goal we have.
We should not basically forget that
chemotherapy is AB side effects,
but targeted therapies have side effects too,
Situation where we are really,
and so we should not.
Situation where we are really,
completely disparaging.
Chemo too much as it’s as some real
basically benefits for for some of
the patient and for chemotherapy
as well As for cell therapy.
I think we need to see the big picture
and how we can sequence and combine these different modalities of treatment. Rather than being one again the again the other.

Awesome, so I think we have reached 1:00 o’clock or one minute past 1:00 o’clock tomorrow.

Francine Natalia thank you for the fantastic presentation, Charlie. Thank you for hosting us and thank you for everything on behalf of everybody in immortality. And thank you to everybody who’s attending.

Yeah, phenomenal work. I just think about in my tenure what’s been going on in hematology.
00:59:51.060 --> 00:59:53.056 Yeah, it’s really exciting.

00:59:53.056 --> 00:59:55.551 So congratulations to all the

00:59:55.551 --> 00:59:57.881 speakers and all the investigators

00:59:57.881 --> 01:00:02.411 and staff working on this. No. OK.