To this week’s character center Grand rounds, we have two speakers today, both from Yale will give us some exciting discussion of some of the work we’re doing here. Our first speaker is Mario Strozza busco. He’s a professor of medicine, director of the liver center. He received his medical and PhD degrees in Italy and then had a number of leadership positions at the University of Milan before joining our faculty. He’s an expert on the care of
patients with liver cancer, is internationally known for his work and hepatology. Liver transplantation is a member of several scientific societies in Europe in the United States. His current research relates to the pathophysiology of biliary tract disease is repaired. Biology of liver repair, liver transplantation, liver cancer in healthcare management, and so today we’re going to hear from Mario and tell of his talk is liver cancer, clinical care and research at Yale.
So Mario, you’re up. Thank you very much, Dan, for the introduction and thanks for the Cancer Center for the Invitation Ann.

And thanks a lot for this Milo. I’m really only as a spokesperson for a group of colleagues that are interested in India in the liver cancer and treating liver cancer. So I’m just the messenger. So what do we do in the liver cancer program we take? We take care of patients with liver masses either benign or malignant are,
and the two most frequent.
Primary liver cancer are able to sell cash. You know my also called HTC and
Intraparticle Angela carcinoma and I focus my talk today mostly on ATC,
which is the most important primary. Cancer of the liver. The liver is an organ which
is located in the abdomen, but really here it is.
The main regulator of the whole body, metabolic coma stasis,
and in fact if the liver fails we actually, the patient suffered of a syndrome which is very bad.
Absolutely Poly systemic syndrome. As you can see here. And the important thing to understand is that 85%--90% of the patient with able to sell casino. They are also cirrhotic in the liver and not only that, but if we follow a cohort of patients with viral induced liver disease either B or C for enough time, we see that the main the. When they die, most of them they died with the in a particular casting armor as shown here. So why what the about the circus number is actually only rise
00:03:08.358 --> 00:03:11.358 worldwide and the estimate are there.
00:03:11.360 --> 00:03:14.629 There are 830,000 cases recorded every year,
00:03:14.630 --> 00:03:16.970 with the mortality that almost
00:03:16.970 --> 00:03:18.374 approached the incidents.
00:03:18.380 --> 00:03:22.079 And why is that? Well, this is the.
00:03:22.079 --> 00:03:25.917 A result of a number of worldwide the
00:03:25.917 --> 00:03:29.289 epidemics that are also risk factor
00:03:29.289 --> 00:03:32.702 for chronic liver disease and among
00:03:32.702 --> 00:03:37.042 them we can mention viral appetite is B&C.
00:03:37.042 --> 00:03:40.294 You see that they the infection
00:03:40.294 --> 00:03:43.028 from viral potatis is hundreds
00:03:43.028 --> 00:03:46.549 of millions of people I call is
00:03:46.549 --> 00:03:49.318 another important work by the.
00:03:49.320 --> 00:03:52.015 What is factor as it is obesity,
00:03:52.020 --> 00:03:52.646 diabetes?
And more and more, we realize that if an important risk factor is due to inequality's an patient population that are underserved and they have difficulties in reaching and being reached by the best care, other risk factors, smoking alpha toxin and an other as well. And this is important to understand that the combination of risk factor increases. And actually the risk. So in every patient that we see, we need to look for all of them. This risk factor are distributed unequally in the world wide. For example, aflatoxin is more frequent
as it goes in in the African continent,
but if we go to the US, All told,
this publication shows Nash is a main factor.
It is actually we have all the
respect or combining here because
we have Nash with alcohol,
we have appetite is C.
And so on. And in fact,
And if we look at the distribution of
the incidents of ATC in the US.
We see that is actually particularly
hygge about 8. Per 100,000 in the.
Massachusetts, Connecticut and New York.
So if we look back more.
In depth into it,
we see that in the US the liver cancer incidence has increased almost three times in the last 30 years, and the mortality is increased almost two times as shown.

Also in this graph on the right, if we look at the numbers and compare the number with two big, GI killers in their adjustable system, like bankers and call, and we see that in Connecticut we have a record of 480 cases per year and this is a combination between HCC an intra Patrick.
so we have 480 new cases and $320

unfortunately and this is a figure which is similar to another big killer like the pancreatic cancer.

730 and 520. So what?

How does the molecular pathogenesis of apples for casino?

We have said it.

Most of the patients have cirrhosis and in fact the main theory is that in the cirrhotic nodule there are Even so happens that brings to Korando casino man.

I’m in one of these is the.
TR T promoter that basically.

Blocks the ability of the liver cell under information to undergo senescence and an among them.

There are other possible.

But the genetic event like P53, which is basically associated with aflatoxin, better cotton imitation.

But this is a scenario that is not very well understood.

All we can say for now is as there are two different classes, one name proliferation,

the other non proliferation that are different in terms of their prognosis.
and in terms of their ability to respond eventually to immunotherapy. So I put the cell carcinoma is a very peculiar cancer because he has a dual personality. It’s a cancer in a failing vital organ and it can be seen from a biological perspective. There are inflammation induced phenomenon, oncogenic viruses, literally natural general mutational landscape and this brings to a complex tumor phenotype with the witches aggressive. It is a terror generals with a high recurrence rate.
When is Sonic Liquor point of view?

We have any plastic disease and the liver disease, and so the street.

The treatment strategy has to be tailored according both to the tumor stage and the function of stage liver disease, and this creates some of the peculiar things in that management of this disease. So we don’t have one single way to manage it that you have resection or ablation came embolization value addition therapy. Systemic therapy still has a role.
we have the possibility to transport the patient.
The only solid organ that can be transplanted and most of these patients actually die because of liver failure and in fact one professional figure that is involved in this.
It is the hepatologist.
What, because of all this, different professionals involved in this in the treatment, the entry points usually are multiple and this multiple entry points in the system creates different trajectory for the patient with way.
Dispassion of resource is an impact on the outcome because there is a confusion and you don’t really know what the part where the patient should follow. And this is one of the reasons why it is important to have a team work. So to give an example, probably will take the whole day to this guy to figure out how to change the tires, whereas the Formula One team can do it exactly in 2.5 seconds. Which is amazing and is this love? Is this out of their coordination of care? So treatment of Apple Circus nominees, coordination of care, and this is the trajectory that the
program has followed through the year.

So we started as a conference and I remember this few people with me wrong. Salom Jeff Pollack. Jeff Wayne Rubber Dam part starting this little room and then he grew to a tumor board. Thanks to Tamar Daddy and then now it’s becoming a program. And maybe it’s really it’s ready for the next step. So when it became a program we designed in IDL structure, which is the patient can come into the system through a single point.
Still working on that aspect,
and then it's actually discussing the tumor board where they treat him,
allocation happens and is allocated to the different specialty according to the best treatment are an.
After that it gets follow-up be 'cause we need to treat the risk factor.
We need to mind the liver.
Help us some chemo prevention protocols and mirroring this clinical operation.
There is also research component which is again a team effort.
So where are we? So we begin with the.
This is a map of the Smiler Care center OK and this is the two main site for
liver care here at again you have in hospital and the VA off without but through the recent year there was open a site in in Bridgeville with magnetic so insight in the ambari came to stand for my shift key. James Mattis T is, you know, the westerly side and soon Alan Jaffe will go to West for now. This is in combination with with the transplant team the with the transplant team with which we have a very good long standing collaboration. Now it really takes a village to treat
this cancer and here you can see. Not all of their colleagues that participates and I have to say it’s a real privilege to be able to work with these individuals, and they are extremely skilled. All of them are leaders in their own right are in their own field, and so the discussion that we have are so enlightening and we follow a structure of discussion going through and analyze the reception, the transplant candidacy, the OR whether we need to use local regional treatment like ablation, radiation.
It’s I don’t have the time to go into this, but it’s every single all of this possible treatment is very complex and the decision making is very complex because it depends from systemic and local factors, and in fact we really an. We basically follow the Barcelona Liver cancer treatment, which is a. but it really has a lot of troubles. OK, there are changes. This is the latest version and takes into account liver function, performance status and then
atomic location of the cancer.

But really there are lot of troubles and we cannot be so strict with the categories and for example this was written in 2019. Now the first line treatment cannot be only confined to patient at about to die, as in this staging system, so a lot of things have changed and that made difficult by the fact that we have multiple theology at the underlying liver disease. The frequent comma abilities in fact, this is a cancer.
That picture above 65 years of age. Multiple treatment option and 70% of them have a recurrence of the cancer in the next 20 months. We have liver transplantation and other actors, so the only way to maintain a structure approach this is to that room and board with four hours is not a way where we present strange cases is really the machine. Ann and the credit for this goes to my colleague and friend to Mark Addy, who set it up and now we discussed 13 cases each week.
Last year we even with the kovit

we discuss 520 cases and one of the busiest actually tumor Board 2 of 200 of them with new cases we have.

300 patient and follow up.

150 new cases and these actually treated in several different ways,

but this is not the venue to to go through the volumes or to their substantial.

The tumor board is also where we got ideas for research and ideas

got ideas for research and ideas

for improvement and innovation.

This is that list of items that we discussed at the last steering committee.

For example,

several of this question that I'm
00:15:06.390 --> 00:15:10.530 not going to read all of them, but.

00:15:10.530 --> 00:15:13.498 Generate. Recent opportunities.

00:15:13.498 --> 00:15:15.550 Anne Anne, Anne, Anne

00:15:15.550 --> 00:15:18.150 Anne and also great care I I wanna

00:15:18.150 --> 00:15:20.180 go briefly through this case.

00:15:20.180 --> 00:15:22.665 This was a patient. Refer to doctor.

00:15:22.670 --> 00:15:24.770 She’s key for transfer evaluation

00:15:24.770 --> 00:15:27.328 Mike so the patient realized that

00:15:27.328 --> 00:15:29.248 he had actually liver cancer.

00:15:29.250 --> 00:15:30.930 And Moran had infiltrative

00:15:30.930 --> 00:15:32.610 hepatocellular carcinoma with with

00:15:32.610 --> 00:15:34.849 the tumour portal vein thrombosis.

00:15:34.850 --> 00:15:37.818 So we discussed the case at the

00:15:37.818 --> 00:15:41.063 tumor board and it was decided that

00:15:41.063 --> 00:15:44.530 there was no other option rather than

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medical treatment or offering a trial. Stacy did try to give him softening by the beginning I, but this was denied by the insurance and so it happened at Stacy adjust open atrial at the initial trial with a diesel Bev, which is now you know, the first line treatment for back in that time was actually we were very lucky that we could offer him and as you see here. In the graph of plotting the alpha fetoprotein, he had a complete response. But in the next two years,
this patient was completely and the quality of life of this patient, which was completely altered by recurrent severe episodes of portosystemic several opathy. As you can see here from the ammonia and actually in during one of these emission it also discussion about goals of care was initiated, so we had a patient who was treated by so we had a patient who was treated by with you from this malignant tumor. But he was dying because I believe this is an act. very bright hepatologist wanagas. intervals with system are in,
another is stalled. Slacker, which is an interventional hepatology calling, decided to embolize his plane arena. Shanta and now the patient is functional cancer free, happy. And when he refers to what happened with the insurance, he quotes wisdom churches saying pessimist sees difficulty in every opportunity, an optimist sees opportunity. So this is a case which we learn a lot about it an in fact. Now particularly,
one of the things that was interesting in the Gary case was that he never had a recurrence as I said occurrences.

In their first two years, so that prompted the opening of a try again by Stacy and Distria will actually try to address the role of adjuvant treatment after surgery or ablation.

Another trial is being brought here by David Madore.

Fu actually addresses and
other nuances of this, so his aim is to understand whether there is a benefit in what we call combination treatment. So the idea to combine embolization with the. Even on Koleji, in combination with a PKI. And another important aspect of the program is the fact that we really tried to record and measure the outcomes. My tarantula Shapiro at there are curating a database of 1000 patients in India and the survival code divided by BCSC states that you see, here are our own. Ariel's affair with John awfully.
Make the termination letter based on.

Now our environment in expertise and is simple example that the outcome is outstanding up to more than three years for this campaign patient with initial cancer, things are changing after this and there’s a lot to be discussed in among these patients and I don’t have it here, but if anybody has a doubt about transplantation, I can tell you that the code was transfer stations like this so outstanding long term. Result for the few patient again get it, but this is a very,
very important aspect of what we do

an it’s going to be so complex

that in fact Julius with Jim Duncan

Manderly and John actually very much

involved in trying to understand

the use that we can have artificial

intelligence in the diagonal.

This characterization treatment of this

Council and we expect that this would

be a great aid to our decision making

and also discovery of new approaches.

So what the liver cancer program

doesn’t have a formalized?

Visas program but is actually

the assembly of of several

different interrested people.
What have we done to put together these people so the first thing that we have been doing with Julius De Mar is these liver cancer talks their monthly in the late afternoon on Thursday. Each of them with two or three percent Asia and this has to be ongoing. Research are now published work. It covers all the aspects, clinical, translation and healthcare and this actually this approach Spark collaboration. There were paper grant application and also a big step. Forward was at last October when again.
with the help of the Miami Justice Ann,
and thanks to the help of Gary Honeycutt’s
and his team in the Cancer Center,
we put forward the first liver cancer
Super Summit which is called pre
Lude because he was not in person.
Where was Virtu are,
but the mission was to address the
Uncle logic challenges or liver cancer
to the collaboration amount of abide.
Spectrum will be a faculty.
And I’m gonna really run through
some of this visa suspect and what
in what I call the Commonwealth to
liver cancer is at yeah OK because
it’s not again formalized structure,
but is the gathering of interested people coming from the medical school, the School of Public Health? the VA system involving departments like surgery, internal medicine, the Cancer Center, the year, liver cancer, the Department of Pathology and so on and so forth. But all these people actually. In a 2019-2020 publish it 72 papers, an 38 of them original article 7R position paper 14 reviews and 14 of them are actually publishing in journals with an impact factor around or above 20,
which I think is pretty remarkable.

So just a very quickly glancing through it.

The number of our faculties are actually involved.

In studying the different risk factors that I mentioned before, so we have outstanding work performing virally theology, interaction with aging, the HIV.

We have food program that addresses the obesity, diabetes and affolder alcoholic liver diseases in other regions branch which is growing an Ann and also health care disparities.
An for example.

Razor, osean and other faculties are addressing.

Some of the. Differences that we see even in connecticu.

So for example, as you can see here. The incidence of HCC is clearly higher in this panic and black population and hopefully will will try to nail down what the causes are.

So outstanding results in outcome research, mostly addressing the role of surveillance and all of.

Antiviral treatment and the growing group of faculties are
also interested in concert cost,
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We do a lot of things,
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but we don’t really know their value
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so this is another growing area.
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Translation studies that also growing and
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just to mention several faculties in Basic,
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more basic studies are interested
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in the transition between Nashville,
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roses and and cancer and in human
NOTE Confidence: 0.8397243
Hansa ran and a lot of people
NOTE Confidence: 0.8397243
is actually interesting in the.
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Role of the tumor micro environment.
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Which this is, I think,
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is very interesting.
This is staining for Alpha, SMA, identifying fiber, associated fibroblasts in cholangiocarcinoma and in hepatoma you see two very different.

Pathology Ann and these are correlated to two very different aggressiveness.

Also the tumor let me very briefly mention some of our work in the macro environment or the calendar carcinoma showing the central role of calf or determining several of the aspects of the two Moran now our Co other
colleagues are addressing this using single cell transcriptomics. This is also an interest of our colleagues in radiology. They’re trying to use the tools of radiology to generate reliable imaging biomarkers for immunotherapy. This is, I think, it’s granted or or or proposed for the NIH by David matter of MGM Duncan interest on the metabolic aspect is also. Followed by by Michael Nathanson, lab, and here is work from Emma tells where I’m like nothing. So I’m looking at the IP3 receptor and mitochondrial functionality in 80C and CCA,
and they're all in the chronic effect like existence of up doses or generating up talking factor of this was published very well last year and finally mentioning. Tell you who, just join and the chair of pathology is, you know, a very well renowned liver cancer researcher and is doing several things. Among this he explaining to detect circulating metallated DNAs as an early diagnosis. Wait, you see, and we're really looking forward very much to this study is an also.
He is trying to use Kartiana Glypican 3 as a target. Hopefully not that big of a TC and I'm gonna finish now because the time is over. But you know this is just an example of the richness of the research that we have. And really this is and I have to thank all the departments that are involved in this enterprise and. You know each of these departments. There are some hepatologist hiding there and this is what what will I call your liver, which is a very old tradition. Here is going to celebrate
the Diamond Jubilee.

Next year and I thank you for your attention.

Thank you very much, Mario.

Very interesting talk. Are there any questions from the audience?

I can start with one.

So recently drugs have been developed that will cure hepatitis C virus.

People are being treated by these drugs.

What fraction of people in this country are affected?

People are being treated by these drugs.

And what’s the effect on liver cancer?

Tell the the strategy would be worldwide application of HPV and therefore I would say that a growing
amount of patients she is being treated should be treated that has had like a slowing down during the COVID crisis but should resume full time. The question of the effect on liver cancer is a very good question because there has been a great controversy because a lot of patient. After eradication of the virus, have the path surprised that delivered Carson happens. Anyway, this is happening in patients that were treated already with significant fibers in their liver. And it was initially proposed that actually the allocation of
the virus would get rid of some kind of beneficial information, but further studies have shown that actually the risk is decreased, but it’s not zero. So why is not zero is something that we need to understand. My personal opinion is that we are simply eliminating one of the many risk factors. You know the regular guy is a guy that didn’t know to have actitis is a little overweight, has smoked. Is drinking, you know, not drunk but enjoying the wine. 
It just doesn’t know it an an therefore yeah, will you ever you have four risk factor of which you eliminate one? This is why this is a internal medicine. This is right because you really have to address all the risk factor in every single patient. Otherwise, you may fail like like the eradication of appetite is C shows in certain patients and so the basic clinical recommendation is that the patient that you were ever advocated while he was erotica still needs to undergo the six months. Screening and surveillance for ACC.
Are there other other questions?
OK, with that I do see the vineyard behind your folder there in moderation.
Yeah moderation, OK thank you.
Thank you very much.
Thank you, thank you.
So our next speaker today is Jonathan Levinthal.
So Jonathan is assistant professor of Dermatology and the director of the Yale Uncle Dermatology Clinic.
He received his MD degree from New York University and is residency here at Yale.

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He specializes in caring for patients with skin cancer, beginning with skin screening programs to detect cancers and sun damage and optimize prevention and therapy. The clinic serves a dermatologic needs of cancer patients dealing with a variety of skin issues, including skin changes due to chemo therapies, can infections, cancers involvement in the scan, radiation, dermatitis, and other changes due to radiation, so we’ll hear that today. So Jonathan I’m looking forward hearing you talk. Thank you.
Thank you so much and it’s a real pleasure to be here today. So today I’m going to talk about dermatologic conditions in cancer patients, and I’m going to provide updates from the ankle dermatology program. So here is a list of my disclosures, mostly from serving on advisory councils with fellow Aqua dermatologist throughout the country looking at skin toxicities as well as some clinical trial research funding. So the objectives of the talks I wanted to start by introducing you to the Aqua dermatology program.
Then I wanted to discuss the importance of cutaneous toxicities and how they can impact patients quality of life as well as their cancer therapies. When severe, I wanted to highlight some of the most common toxicities that I see from select targeted and immune checkpoint inhibitors and also traditional chemotherapy. As well and discuss the role that aren’t with their mythology.

So for some background, the Uncle Dermatology program was established by my great mentor and friend, Jennifer Choi.
Shortly after she graduated residency and then I had a great opportunity when she got recruited to Northwestern as a chief resident to start seeing patients in the clinic for which I’ve led the clinic ever since. And we’ve really seen a tremendous outgrowth of support from so many colleagues in Metanx terjung Radon, an anthology, and the clinic has really grown dramatically over the years. It’s a very robust, busy clinic. Some days we see up to 50 patients. And I just have a great team of
nurses residents as well as research fellows and support from the Yale Center for Clinical Investigation.

So the field of supportive Uncle Dermatology really blossomed in the 1990s with the advent of many different targeted kinase inhibitors, which skin toxicities were so common in almost the majority of patients and it really encompasses many different things that we service, so there’s definitely all the toxicities that we see from the systemic therapies, radiation therapies, graft versus host disease as well as complications from cancer.
00:32:43.280 --> 00:32:45.260 Going to the skin with metastases,

00:32:45.260 --> 00:32:47.640 but there’s really a lot of other

00:32:47.640 --> 00:32:49.356 indirect complications that we treat

00:32:49.356 --> 00:32:51.276 in clinic and that includes paranoia.

00:32:51.280 --> 00:32:52.724 Plastic disease, infectious complications,

00:32:52.724 --> 00:32:54.529 especially in patients who are

00:32:54.529 --> 00:32:56.317 immuno suppressed as well as being

00:32:56.317 --> 00:32:57.692 part of the survivorship program.

00:32:57.700 --> 00:32:59.305 For many patients who have

00:32:59.305 --> 00:33:00.268 survived cancer now,

00:33:00.270 --> 00:33:02.140 an increased risk for developing

00:33:02.140 --> 00:33:03.636 cutaneous carcinogenesis and then

00:33:03.636 --> 00:33:05.737 also part of the umbrella is that

00:33:05.737 --> 00:33:07.329 the Melanoma program I’m part of.

00:33:07.330 --> 00:33:09.376 It falls under the umbrella of
Uncle Dermatology and so a lot of what I do is also high risk in cancer screening to diagnose and treat many different types of skin cancers and also collaborate with the cancer genetics program to obtain tissue for genetics. So wanted to start by discussing the cutaneous toxicities are not just cosmetic. These are really important issues that impact patients quality of life and there’s been many studies over the years looking at validated quality of life surveys. It’s just so common for these...
toxicities to impact in both physical as well as emotional domains and so one interesting concept is that women seem to be affected greater than men in terms of their quality of life and it’s probably because of the types of regiments they did receive for breast and other gynecological cancers which frequently impact the here in the nails and so this can affect women’s self image, cultural identity, sexuality as well as mental health, and a loss of control over their body.
The hallmark examples

which we see from the cytotoxic agents,

in particular an one homework study,

showed that almost 60% of women with

breast cancer preparing for chemo

considered this to be the worst

and almost 10% even considered

delaying treatment in fear of it.

So these are real,

very real and important issues,

there’s been so many other studies

looking at the acne, acne reform,

ranch hand, foot rashes,

nail changes in mucus, itis,
all of which I’m going to discuss in which can impact quality of life. So the study on the left kind of highlights an important concept that it’s not just those main toxicities that can impact patients quality of life. In this study of targeted agents in breast and colorectal cancers, you’ll see that things like itching, dryness of the skin, easy bruise ability, pigmentary changes, they can all be associated with poor quality of life and the study on the right looked at different types of chemotherapy and
how they impact quality of life.

And not surprisingly.

A lot of the more novel, targeted therapies, especially the EGFR inhibitors, were associated with an increased number of skin toxicities, but also those which impact quality of life greater than some of the traditional chemotherapeutic agents.

Unfortunately, there's mounting data showing that early dermatologic intervention can really make a difference, and so Uncle dermatology programs have been showing up at most of
the premier cancer centers in the States and abroad, and one study from MSK show that with outpatient dermatologic involvement, patients on immunotherapy were less likely to have interrupted treatment 5% versus 30% to those managed without dermatologic intervention. In a recent study by the Harvard Group similarly showed. The inpatient consultation can also decrease the chance of patients receiving systemic immune suppression and immune therapy discontinuation. Now,
we haven’t performed a comparative study.

We did perform a very large study recently that was published of over 100 immunotherapy.

Rash is 1/4 of which presented to my clinic, often with disruption of immunotherapy.

But with early dermatologic intervention, over 90% of these patients were able to remain on their treatment, so I think these numbers are compelling.

I see from targeted therapy. I mean there’s so many different types of agents to discuss,
review some of the main ones.

In the interest of time so the EGFR inhibitors are a class that are commonly associated with cutaneous toxicities. Not surprisingly, as the epidermal growth factor receptor is expressed in the skin, hair and nails, and really important for homeostasis and some of the monoclonal antibodies likes to talk some mad panitumumab as well as the 1st and 2nd generation drugs. Fortunately, the third generation Presents with cutaneous toxicities in the majority of cases.
drugs like OC murdered him for a lung cancer patients. They don’t seem to get the rest, probably less than 30%, and so the most common toxicity that we see is the papulopustular for the acne or form rash, and this usually manifests on patients face, scalp, chest and back. Although it could be widespread and one common misconception is that it’s just a sterile technique. Reform drug eruption, which is true. However, I find a large percentage of these patients.
 Especially when they get to higher grades

Both M RSA an MSA,

so that’s a good therapeutic Pearl

to obtain wound cultures and hear

each year is crusting.

It was all in petition eyes with staff.

Oreius is a more typical scenario

in one of the more robust severe

toxicities that might require

more aggressive treatment,

which I’ll discuss.

We see lots of nail infections

paronychium and because of the
piercing of the nail plate into the hyponychium patients can get this friable granulation tissue known as pyogenic granulomas. These can be exquisitely tender and painful and definitely impacts patients quality of lights. It's not uncommon to see her growth abnormalities, including elongated eyelashes. Some patients have a hard time trimming their eyelashes, which are curving inward and irritating their eyes, so they'll just see me analysis them with cutting their
00:38:13.373 --> 00:38:15.893 eyelashes we see lots of dryness and painful cracks and fissures too.

00:38:17.750 --> 00:38:19.330 There is an example of, you know a patient who presented with a neck near former option which was in petition eyes with staff.

00:38:21.058 --> 00:38:23.288 She responded quite well to Doxie, cyclin topical steroid ointments, antibiotic ointments.

00:38:25.328 --> 00:38:27.226 And I'm a big fan of antiseptic soaks like aluminum acetate removed serious crusting.

00:38:29.169 --> 00:38:31.069 Here's another example of a patient. And I'm a big fan of antiseptic soaks like aluminum acetate removed serious crusting.

00:38:33.869 --> 00:38:35.760 Also recently from the Lung Cancer Group who also had quite a severe

64
acne deformed mesh occasionally in very severe circumstances there can actually be associated alopecia as well. She responded very well to dermatologic intervention. I wanted to highlight that. While the acne reformers typically presents during the first few weeks on the head, chest and back, we have seen uncommon presentations as well, which are described in the literature and those are prepared drug eruptions which likely fall into the category which likely fall into the category of the late acne reform toxicity. In these cases usually present many months into treatment,
and they often present on the lower extremities in the buttocks, and as you can see with these perperek looking lesions, and they’re also frequently infected with staff on Moon culture. Here’s an example of a patient with head and neck cancer who responded to dermatologic intervention. And here’s an example of a patient who has pretty typical pyogenic granuloma with Paronychium, who responded to the topical beta blocker timolol gel. Many of these cases are non responsive.
to conservative approaches and sometimes procedural intervention may be required, like using silver nitrate to court arise

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Here they’ve been looking at lots of new novel approaches for treating the rash, none of which are really gained widespread use.

Some of the data is very mixed with these drugs and so we definitely need New approaches and then I just wanted to briefly mention that there’s a few clinical trials which we’re doing here. Studying the rash one is currently recruiting and I really appreciate my awesome collaborators in the head and neck and thoracic group which are helping to recruit patients. And that’s to better understand the
microbiome of the populations or option
NOTE Confidence: 0.78627217
and see how changes in the microflora
NOTE Confidence: 0.78627217
can be associated with the severity of
NOTE Confidence: 0.78627217
the rash and response to rash treatment.
NOTE Confidence: 0.78627217
And then there’s a company that we’re
NOTE Confidence: 0.78627217
working with that’s developing a
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novel probiotic with staff epidermal
NOTE Confidence: 0.78627217
disappointment to look to see if
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this is going to reduce secondary
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infections with staff wareus,
NOTE Confidence: 0.78627217
which are commonly associated
NOTE Confidence: 0.78627217
with severe rashes.
NOTE Confidence: 0.78627217
And so this is in development
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hoping to do this trial next year.
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So shifting gears,
NOTE Confidence: 0.78627217
I wanted to briefly discuss
other targeted agents, which we see a lot of toxicities from in the breast group. They heard two inhibitors as well as American hitters used for various cancers can actually share some of the properties of the EGFR inhibitor. Reactions will often see folliculitis, eruptions and acne or form rashes. However, they usually less severe and less frequent. I wanted to talk about another very important toxicity which comes to clinic and that’s the hand foot skin reaction.
So these usually develop from the anti-angiogenesis agents, some of which we just heard about which are used in the paddle cellular carcinoma such as the anti-VEGF agents. And here’s a list of the FDA approved ones and so this seems to be one of those toxicities which just so frequently impacts patients’ quality of life. They have a hard time being able to work to do their daily routine. It very often impacts their activities of daily living. Patients usually present early on. We just kind of thickening or hyperkeratosis of the palms and soles,
but then over time they get these very painful. Callous is, sometimes they are inflamed and then in the severe cases we even see blisters develop as well. This rash can be associated with very painful dysesthesia with sometimes will use gabapentinoids like pregabalin or gabapentin to help assist with at this stage as well. These drugs also are associated with genital eruptions as well as splinter hemorrhages on the nails. So we don’t really have great treatments
for the hand foot skin reaction right now.

Unfortunately, many patients don’t respond to moisturizers and karata lytic,

so dose reduction is often needed.

So we’re doing a study looking at a novel topical nitroglycerin ointment to treat grade two or grade three hand foot skin rash and the first phase is going to be comparing it to vehicle and then the second phase.

Comparing pyren lower percentages and so if you have any patients who present with hand foot skin.

On these approved drugs on the left...
really most patients eventually get to grade 2 because it’s almost always interfering with her activities of daily living. Please please I’ll refer them to our study. We definitely need to do better in managing this toxicity. In interest of time, I’m just gonna I’m just just briefly highlight that we could spend all day talking about the different targeted agents in the toxicities I see. Here are some examples just to illustrate that really many different classes can do it. Since you were on or Brewton if for
CLL often get perperek eruptions,

NOTE Confidence: 0.7819162

folliculitis patients with breast

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cancer on PR, 3 kinase inhibitors,

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and get really terrible.

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Morbiliform exanthems some requiring

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the use of Prednisone so wanted to turn

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now to immune checkpoint inhibitors.

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Because I think you pennis

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toxicities are really important.

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To discuss with this class

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of cancer cancer therapy.

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And so all great rash,

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plus parictis it kind of tally.

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It all can occur in up to 50% of

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patients on checkpoint inhibitors at one

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point in time during their treatment.
This is especially true of patients who are on combination CTL, a foreign PD one therapy and the way that I think about the toxicities from the checkpoint inhibitors is categorized them into those that are the most frequent that we see which are the morbilliform rashes, the lichenoid rash, which I'll discuss a bit more about the exame and the parictis as well as psoriasis. And then there’s the whole category of autoimmune disorders which occur as immune related adverse events such as diddle I go and bullous pemphigoid.
which I'll discuss more about as well.

Fortunately, the severe rashes, the life threatening Stevens Johnson ones we've seen them, but they're not. They're not common, and then there's kind of the miscellaneous category of those that are granulomatis like sarcoid for those involving the panniculus or the fassia. So this is actually one of the largest studies out there. Looking at the different branches from in therapy that we published a couple of years ago and it was a retrospective retrospective study.
of over 100 rashes that we saw in the ankle during clinic and we found is that they really have many different clinical and histopathologic morphologies here and a lot of them resembled idiopathic dermatosis that we treat in dermatology. For patients who are not on checkpoint inhibitors. If you take a look at the yellow box I highlighted kind of the top five and what’s interesting about this is that a lot of these common rashes actually develop many months into therapy. The most common one can be sometimes...
six months into treatment, and I think that’s important because patients don’t always realize or put together that their new rashes because of their immune therapy, and in some of the oncologist who are less familiar with these toxicities, also may not. And so I think that’s important to keep in mind that you can definitely get late toxicities to write. This is a very prominent feature. In most of these containers, toxicities fortunately were able to manage these patients in the vast majority of time,
00:45:45.400 --> 00:45:47.560 topically by 20% of patients required Prednisone because of the severity of the rash and 25% had disruption of immune therapy at some point, sometimes before they saw me in clinic, or sometimes because the rash progressed. But really, the vast majority can remain on immune therapy. It was just the cases of Stevens Johnson, a really bad bullous pemphigoid where immune therapy was discontinued and another important concept here is for the rashes. That do recur after Prednisone or that persist.
Targeting the dermatosis in a more efficient way is probably going to be the future of how these rashes are treated and so we’ve had a great deal of success using things like asset reading for the psoriasis or lichenoid rash. We use Alisme after methotrexate for the Bull’s tendency. More recently for cases that are not associated with checkpoint, I wanted to take a moment to discuss that. What is the lichenoid dermatitis?
NOTE Confidence: 0.8337146
00:46:41.405 --> 00:46:43.509 is we throw around the term lichenoid
NOTE Confidence: 0.8337146
00:46:43.509 --> 00:46:45.195 alot in dermatology and I’m not
NOTE Confidence: 0.8337146
00:46:45.195 --> 00:46:47.172 sure if the if our colleagues in
NOTE Confidence: 0.8337146
00:46:47.172 --> 00:46:48.792 meddock or familiar with it and
NOTE Confidence: 0.8337146
00:46:48.792 --> 00:46:50.888 so like in what looks like like in
NOTE Confidence: 0.8337146
00:46:50.888 --> 00:46:52.665 which an Organism that grows on
NOTE Confidence: 0.8337146
00:46:52.665 --> 00:46:54.782 trees kind of scaly and crusty looks
NOTE Confidence: 0.8337146
00:46:54.782 --> 00:46:56.564 kind of like the rash does.
NOTE Confidence: 0.8337146
00:46:56.570 --> 00:46:58.232 And then there’s the histologic term
NOTE Confidence: 0.8337146
00:46:58.232 --> 00:46:59.979 of lichenoid dermatitis which is an
NOTE Confidence: 0.8337146
00:46:59.979 --> 00:47:01.449 interface dermatitis with the bandlike
NOTE Confidence: 0.8337146
00:47:01.449 --> 00:47:02.590 infiltrate of lymphocytes ANAN.
NOTE Confidence: 0.8337146
00:47:02.590 --> 00:47:04.708 This is the most common histopathologic
NOTE Confidence: 0.8337146
00:47:04.708 --> 00:47:06.899 finding that we see in the skin.
NOTE Confidence: 0.8337146
00:47:06.900 --> 00:47:08.986 And so the lichenoid rash can occur
NOTE Confidence: 0.8337146
in up to a third quarter to 1/3 of patients on PD one and PD Wagon one agents. And this is kind of a more severe example highlighting the pink violaceous scaly patches and plaques. Here’s a patient who responded to Acitretin were very persistent Palmer planter involvement and he did not do as well with topical steroids or even a short course of Prednisone. I also wanted to highlight that this lichenoid rash can involve the mucosa, and when that occurs, it can really be quite severe with ulcerations on the genitals as well as the oral mucosa.
Anan this this this clearly is very painful and we were very low threshold for Prednisone in these cases. Sometimes we try things like hydroxychloroquine in those that persist. So in addition to the lichenoid rash from checkpoint inhibitors, we can also see eczematous presentations. Sorry, acid form presentations. And then there’s patients that just have terrible parictis even without an associated rash. So here’s a typical scenario of a patient with psoriasis, then goes on checkpoint
inhibitor therapy and flares,
and she responded very well to phototherapy,
which is a really nice non
systemic option for these patients.
Here’s an example of widespread eczema,
and here’s a patient that I share with
Doctor Goldberg who just developed just
severe itch and she comes to clinic,
covered in bandages and
and she eventually.
Did somewhat better with pre
gabelein and phototherapy,
so just highlighting that the different
the spectrum of these papulosquamous rash as we call them from dermatology.
So both paperboy is one of those
rashes which is not common, but it’s a very important one because it has a great deal of associated morbidity with it and so for those who aren’t familiar with it, it’s an autoimmune blistering disease with deposition of IgG and complement at the dermal epidermal junction is seen here in my patients tissue sample and patients also make autoantibodies against BP 180, so we conducted a study a few years ago at our uncle during clinic and we found that about 1% of the patients on checkpoint inhibitors
with PD one or PD wagon one.

Based on our pharmacy develop

this rash so it’s not common,

but but it definitely can be quite

extensive and the latency is

also usually four to six months.

Clinically, patients will often present with

just worsening queritis even before

the onset of rash.

Then they get these urticaria lesions

with tense vesicles and bullae,

which can become eroded,

and you can also get mucosal

involvement as well.

Think about the bullous pemphigoid
rash is unlike a lot of the more common exanthems and lichenoid rash. These typically require Prednisone due to the severity of the presentation. We've also had cases which have persisted even after immunotherapy has been stopped, and even after a Prednisone taper likely do too. I'm just immune activation and so for those cases things like Rituxan, MAB formalism, Maverick dupilumab which are biologics, I'll discuss later might be very helpful.
And the one question about that comes up a lot is when to worry about a typical macular papular example, when should you worry about progression of Stevens, Johnson, and so? My advice with these cases is obviously, you can grade it based on the body surface area, but when the rash is pink and pure Riddick. It’s very reassuring when the rash starts to become this more dusky color. And painful. That’s when you really have to worry about a progression to a more severe cutaneous reaction, especially if there is any coastal
involvement or blisters or any systemic signs
or symptoms really have a low threshold
for Prednisone and watching carefully,
we’ve definitely seen these very
atypical scenarios where an example
just progressed and slowly over the
course of several weeks progressed to
a Stevens Johnson type of scenario.
And that’s been that’s been
published with checkpoint inhibitors,
which is actually very different
than classical Stevens.
Johnson would just takes off.
At a very rapid tempo nears examples
of examples that we’ve seen,
00:50:59.420 --> 00:51:01.112 as well as Stevens Johnson from
NOTE Confidence: 0.79727185
00:51:01.112 --> 00:51:01.676 Hippie Niveau.
NOTE Confidence: 0.8119258
00:51:03.830 --> 00:51:05.636 An I think the future direction
NOTE Confidence: 0.8119258
00:51:05.636 --> 00:51:07.612 for it for treating these cutaneous
NOTE Confidence: 0.8119258
00:51:07.612 --> 00:51:10.090 toxicities is is looking at a more
NOTE Confidence: 0.8119258
00:51:10.090 --> 00:51:11.810 efficient way to shut them down.
NOTE Confidence: 0.8119258
00:51:11.810 --> 00:51:13.082 Basically treating the dermatosis
NOTE Confidence: 0.8119258
00:51:13.082 --> 00:51:14.672 in the most targeted approach.
NOTE Confidence: 0.8119258
00:51:14.680 --> 00:51:16.290 There’s definitely a good amount
NOTE Confidence: 0.8119258
00:51:16.290 --> 00:51:17.900 of data suggesting that the
NOTE Confidence: 0.8119258
00:51:17.956 --> 00:51:19.456 use of systemic steroids is,
NOTE Confidence: 0.8119258
00:51:19.460 --> 00:51:20.560 in general, fine, inappropriate,
NOTE Confidence: 0.8119258
00:51:20.560 --> 00:51:22.629 and it has has not been shown
NOTE Confidence: 0.8119258
00:51:22.629 --> 00:51:24.434 to impair tumor response when
NOTE Confidence: 0.8119258
00:51:24.434 --> 00:51:25.517 treating cutaneous toxicities,
NOTE Confidence: 0.8119258
00:51:25.520 --> 00:51:27.110 but for those cases that
are just recalcitrant, I think we’re going to find the use of anti aisle 413 drugs like the pillow mab or anti Ige. He antibodies like oh Melissa Matthews more frequently. We already have plenty of biologics used in psoriasis and I think there is mounting data in case series of these being used for checkpoint rash as well as TNS for Stevens Johnson. Here’s an example of a patient I share with Sarah Weiss who had bullous pemphigoid which kept flaring when we slowly taper the Prednisone.
Eventually, with the concomitant administration of Melissa Map were able to get the patient off criticism. And so in the final moments, I just wanted to highlight it’s not the forgotten child, because we see lots of toxicities from the cytotoxic drugs. But these I think you’re probably more familiar with because they’ve been around for a long time, but definitely, alopecia mucositis are kind of your hallmark toxicities. Nail changes are really important.
and he’s come up a lot to my clinic, specially young women with breast and gynecological cancers on taxanes or anthracyclines. They get very painful paronychia subungual hemorrhage. They can lose the nail plate they can become. Co infected, and so I think these toxicities are really important and then there’s the toxic rash of chemotherapy which can be hand foot syndrome or malignant intertrigo flow under the umbrella of toxic erythema of chemo and these reactions occur.
through the ecrivain excretion of chemo in the skin of echoing glands. And we just wanted to do a brief shout out to my awesome research fellow who just matched into dermatology at Cornell. Rihanna and she was very interested in looking at the cutaneous toxicities in patients we’ve seen with skin of color which really make up a large proportion of our clinic. And while the diagnosis in general or similar to patients without skin of color, there’s clearly a very prominent finding of hyperpigmentation, which is very bothersome and very,
very prevalent after a rash. Examples of that include cases where patients who get fatal outcomes are associated with darker skin. It's obviously a lot more noticeable, and there's definitely a propensity for certain hair loss conditions, such as alopecia. Here's an example of a patient with keloid overport site that responded well to injection of triamcinolone. It's important to consider how these toxicities differ and in various populations. In conclusion, it's important to refer to these considerations.
patients to our clinic.

I think the short answer is anytime you need a hand, we're really happy to see these patients.

It is a privilege definitely for rashes that are higher grade that are impacting quality of life or that are recalcitrant to kind of conservative management. And definitely anytime there's a red flag that I mentioned like skin pain, duskiness, blisters or plus definitely send those patients our way.

So in conclusion, I hope you'll see from this talk that cutaneous toxicities are not just common, but they're also really important in the
overall management of cancer patients.

I hope that Dermot Earley dermatologic intervention can make a difference.

Remember that the EGFR acne reform rash often starts. It is a sterile rash, but it can often be secondarily infected and you can get these unusual late perperek eruptions as well.

Hand foot skin from the anti angiogenesis drugs and definitely have associated pain. We don’t have great treatments yet, so please consider referring patients to the study using a novel nitroglycerin.
00:54:44.173 --> 00:54:46.224 ointment to treat it and then turning
NOTE Confidence: 0.828433199999999
00:54:46.224 --> 00:54:48.040 to the checkpoint inhibitor rash.
NOTE Confidence: 0.828433199999999
00:54:48.040 --> 00:54:49.804 I think the lichenoid one is
NOTE Confidence: 0.828433199999999
00:54:49.804 --> 00:54:51.710 the important one to know about.
NOTE Confidence: 0.828433199999999
00:54:51.710 --> 00:54:53.588 It’s common it can have associated
NOTE Confidence: 0.828433199999999
00:54:53.588 --> 00:54:54.840 parictis and mucosal involvement
NOTE Confidence: 0.828433199999999
00:54:54.895 --> 00:54:56.300 as well as bullous pemphigoid,
NOTE Confidence: 0.828433199999999
00:54:56.300 --> 00:54:57.830 which frequently requires systemic therapy.
NOTE Confidence: 0.828433199999999
00:54:57.830 --> 00:54:59.666 And if there’s any red flag,
NOTE Confidence: 0.828433199999999
00:54:59.670 --> 00:55:00.585 signs or symptoms,
NOTE Confidence: 0.828433199999999
00:55:00.585 --> 00:55:02.415 obviously you know you have to
NOTE Confidence: 0.828433199999999
00:55:02.415 --> 00:55:04.328 treat these patients aggressively.
NOTE Confidence: 0.828433199999999
00:55:04.330 --> 00:55:06.458 So I just wanted to thank really all
NOTE Confidence: 0.828433199999999
00:55:06.458 --> 00:55:08.708 of my colleagues Ann and Metang.
NOTE Confidence: 0.828433199999999
00:55:08.710 --> 00:55:09.679 Sir John Cradoc,
NOTE Confidence: 0.828433199999999
00:55:09.679 --> 00:55:11.294 everyone at Smilow who’s supported
our clinic over the years.

I have a really great team from the admins to the nurses to my chief residents, many of which have chosen Uncle Dharmas. Akarere Anatomy very proud and as well so my my research fellows, an NYCC I.

So if you ever have any patients, So thank you and I’ll take any questions.

I’m very I’m always available.

You can text me call me.

Contact us and we’ll gladly see them.

Do you have questions from the audience?

My recollection is that with the the B RAF inhibitors there was a serious
problem with squamous cell carcinoma’s is that yeah so actually had a. I had a picture of that slide. I didn’t go into it too much but we had. We saw a lot of toxicities over the years with the beer at inhibitors, but with the concomitant administration we’ve actually seen that basically drop down to near 0 and so you can still get phototoxic rash is another odd things, like everything and awesome, we’ve not seen squamous cells develop in patients on be right contributors to the American hitter.
Coadministration

perfect thank you.

Any other questions?

If not, thank you Jonathan.

Very interesting. Looks like

you’re making a lot of progress in

managing these disorders.

Thanks for having me.