Instead, it is for me a great pleasure to introduce Doctor Tamar Kali, who is now Professor of Internal Medicine and the Department of Internal Medicine, but also the Chief of Gas and Technology and the VA Connecticut healthcare system. And this is not a small place, in fact she. Is there after Harold Kahn, Roberta Grossman and Lupica sits house so she has a great legacy to uphold and we. Certainly, sure. She'll do even even better in the VA system. She directs the cancer program and also has
been very active in the VA system at large.

NOTE Confidence: 0.739211703461538

Where she. Ryan, Sir.

NOTE Confidence: 0.739211703461538

Some very important multicenter trial

NOTE Confidence: 0.739211703461538

among them some already famous like

NOTE Confidence: 0.739211703461538

the vocal other on the statins will

NOTE Confidence: 0.739211703461538

soon be available and and also a

NOTE Confidence: 0.739211703461538

new recent very large grant on the

NOTE Confidence: 0.739211703461538

use of abbreviated MRI to screen for

NOTE Confidence: 0.739211703461538

liver cancer and this is another great.

NOTE Confidence: 0.739211703461538

I could give it to you.

NOTE Confidence: 0.739211703461538

She is a great mentor for a number of hours.

NOTE Confidence: 0.802867781666667

Fellows and trainee and and I like

NOTE Confidence: 0.802867781666667

to think that she has been a trainee

NOTE Confidence: 0.802867781666667

here for many, many years and we

NOTE Confidence: 0.802867781666667

were pleased to see her growth.

NOTE Confidence: 0.802867781666667

So in a way, she is the witness
And how Michelangelo used to say, after she stopped sculpturing the Moses, he said, why don’t you talk? Well, our masterpieces talk, and here I can give you some metadata on the episode casino.

Thanks so much Mario for the introduction. So Mario actually has been my clinical mentor for going on a couple decades now, not quite yet, a couple decades, but. He actually started the first tumor conference for HCC at Yale and I was part of that conference as a trainee. And actually what I learned from him,
I took to the VA.

So we have a really nice network of regional tumor boards which have been incredibly fruitful.

So I’m going to talk about a lot today. I’m hoping to really impart what’s going on in current practice and pearls, but mostly a lot of puzzles. So if you come away with more questions than answers, that’s the objective. There are a lot of questions right now in HC.

And I’m going to talk a little bit about the work we’ve been doing both at Yale and the VA.
I'm a hepatologist and so I may use acronyms you don't understand. I'm hoping I will explain them all, but if you have questions, by all means, don't hesitate. So my objectives are for you to understand the present state really of biomarkers and potential emerging biomarkers in HCC, to understand the importance of multidisciplinary management of HTC and key stakeholders and decision making and to learn about new therapeutics and treatment paradigms. But mostly I think what I'm trying
to impart is just how complex this landscape has become and how essential it is for us to work together both clinically and at the bench. So HTC as you know is a global health problem. This is a map of the world showing the sort of different degrees of blame for certain underlying etiologies of chronic liver disease. In the West it’s been predominantly hepatitis C, in the east predominantly hepatitis B. But what’s really important here is to note the prevalence of fatty liver disease or non alcoholic
steatohepatitis related liver disease
as well as alcohol and the pandemic
has brought to light a lot of issues.
Regarding alcohol and a lot of
sex disparities and alcohol and I
think we're going to be seeing HC's
related to really the synergies of
things like metabolic syndrome,
alcohol etcetera.
So the epidemiology is definitely shifting.
Viral hepatitis will always be a
major issue and until we can you
know essentially do the right public
health thing globally,
we're still going to have happy
you know related HCC.

So HTC is a leading cause of liver related and cancer related mortality.

So there are sort of competing risks of death.

When you think about HTC, you want to think about the person's liver disease as potentially a competition to their cancer.

You can see that it claims upwards of almost a million deaths.

It is the leading cause of death in cirrhosis and 1/3 of patients will with cirrhosis will develop HCC over their lifetime.

And you can see that it claims upwards of almost a million deaths.
By 2025, we think globally will have a million deaths related to liver cancer. And chronic liver disease is really a prerequisite in 90% of the cases. But how much fibrosis is still an issue that we’re studying. A lot of that was due to hepatitis C but the issue is that even though things are kind of steadying from hepatitis C and our ability...
to treat and cure hepatitis C,
NOTE Confidence: 0.903506407857143
the fatty liver disease epidemic.
NOTE Confidence: 0.903506407857143
Sort of the next wave.
NOTE Confidence: 0.903506407857143
So who should get surveillance?
NOTE Confidence: 0.903506407857143
We recommend liver ultrasound and
NOTE Confidence: 0.903506407857143
AFP every six months in all patients
NOTE Confidence: 0.903506407857143
with cirrhosis and patients with
NOTE Confidence: 0.903506407857143
chronic hepatitis B and that’s
NOTE Confidence: 0.903506407857143
regardless of cirrhosis.
NOTE Confidence: 0.903506407857143
And the way that we image people
NOTE Confidence: 0.903506407857143
is essentially with an ultrasound
NOTE Confidence: 0.903506407857143
they should have an AFP.
NOTE Confidence: 0.903506407857143
But if they have an elevated AFP even
NOTE Confidence: 0.903506407857143
if they’re ultrasound shows nothing or
NOTE Confidence: 0.903506407857143
if they have something focal on ultrasound,
NOTE Confidence: 0.903506407857143
we then go to dynamic contrast
enhanced imaging with a CT or MRI. But there are some Gray areas here, sorry, this didn’t convey well the first line of that says hepatitis C with a cure, but without pre-existing cirrhosis prior to their cure, non-alcoholic fatty liver disease without cirrhosis. So these are folks who we really don’t have biomarkers for. They don’t fall into the cirrhosis category and many of them are being diagnosed with HC and they shouldn’t have and aren’t in a
screening or surveillance program.

We know that liver cancer surveillance saves lives.

I'm going to actually use the term screening and surveillance kind of interchangeably here, understanding that we're looking at an at risk population. Those are people with cirrhosis. So it's really surveillance. But I think a lot of people are used to the term screening, meaning that they don't have a pre-existing cancer. And so you're going to screen for a cancer. Just know that when it comes
time to discuss the trial that I'm going to be discussing, we have to call it screening because that's just what they made us call it. But surveillance is really the proper term. So this is a nice graphic of a big meta analysis that looked at almost 150,000 patients and showed that really the benefits of surveillance are manifold. So we can detect cancer early, we can offer curative therapy and we can improve overall survival. There are some sort of data free zones here in terms of the harms.
of screening and these are things that need to be studied in this population and those harms are many different types of harms, financial, physical, etcetera. So surveillance is advised by all GI liver societies and NCCN, but ASCO and the preventative Services Task Force don’t advise surveillance and until there is a mandate for this, it’s not going to be taken up widely by primary care providers and this remains a major issue. So surveillance rates are poor.

So this is actually a private sector study that looked
at a cohort of hepatitis C cirrhosis patients. So they really should have been in a surveillance program and only about 1/4 we’re getting every six month. Ultrasound. So this is pretty abysmal. Of longer surveillance rates, maybe every year somebody’s remembering to do this, but it’s more haphazard than actually being done regularly. Now VA data looks a little bit better. We’re at about 44% and we do have a lot of different ways to get our
00:08:15.963 --> 00:08:18.939 primary care docs to order ultrasounds.

NOTE Confidence: 0.844235941578947

00:08:18.940 --> 00:08:20.830 But I think what’s really important is

NOTE Confidence: 0.844235941578947

00:08:20.830 --> 00:08:23.343 if you compare this to places in Europe

NOTE Confidence: 0.844235941578947

00:08:23.343 --> 00:08:24.944 where surveillance rates approach 65%,

NOTE Confidence: 0.844235941578947

00:08:24.944 --> 00:08:27.216 for example in the UK or in Japan

NOTE Confidence: 0.844235941578947

00:08:27.216 --> 00:08:28.967 where there is high as 75%,

NOTE Confidence: 0.844235941578947

00:08:28.967 --> 00:08:29.681 we’re really,

NOTE Confidence: 0.844235941578947

00:08:29.681 --> 00:08:33.220 we have a long way to move this needle.

NOTE Confidence: 0.844235941578947

00:08:33.220 --> 00:08:34.696 And we really only see the

NOTE Confidence: 0.844235941578947

00:08:34.696 --> 00:08:35.680 tip of the iceberg.

NOTE Confidence: 0.844235941578947

00:08:35.680 --> 00:08:38.360 So in addition to low uptake of surveillance,

NOTE Confidence: 0.844235941578947

00:08:38.360 --> 00:08:39.990 many patients are unaware of

NOTE Confidence: 0.844235941578947

00:08:39.990 --> 00:08:41.620 their risk of developing HCC.

NOTE Confidence: 0.844235941578947

00:08:41.620 --> 00:08:43.628 And that’s due to the silent nature of

NOTE Confidence: 0.844235941578947

00:08:43.628 --> 00:08:45.515 cirrhosis and the lack of awareness of

NOTE Confidence: 0.844235941578947

00:08:45.515 --> 00:08:47.380 the disease among primary care providers.
And primary care providers now are really burdened by so many things they have to think about that liver disease is pretty low on the list. Now we know that linkage to liver cancer care starts with identifying cirrhosis and starting surveillance. But again, primary care providers desperately need to be educated to even suspect cirrhosis and surveillance really needs a mandate. I don’t think this is going to be done until we actually prove that surveillance saves lives, and that probably has to be.
done in a randomized trial.

So at risk populations that I talked about before are changing with the Natural History of liver disease.

So in the US, we are widely treating hepatitis CI would say in the VA we've treated almost 75% to 80% of our patients with hepatitis C. Some 160,000 veterans have been treated.

And so this actually gives us a unique group in which to study post SVR sustained viral response risk of HCC and we’ve seen that risk go down significantly, however, if there's significant.
Fibrosis stage three to four, they’re still at pretty high risk of developing HCC in their lifetime, but we are not seeing that it’s cost effective to do ultrasound in patients without cirrhosis. So the question is, are there other biomarkers we could be looking at? Noncirrhotic Naphill DI think is keeping us all up at night because up to 1/3 of fatty liver disease related HCC occurs in the absence of cirrhosis and these people are usually diagnosed late.
But if you think about the 70 million Americans who probably have NAFLD. There it’s really not cost effective to order an ultrasound for them. So again we need biomarkers and imaging really is, is not the way to go.

So we’re looking at risk stratification tools to identify those at highest risk and then surveillance now in clinical practice is done on a case by case basis. So this leads to the next problem which is that HTC is diagnosed late. So this is SEER data from 2012 to 2018 which shows that you know in the majority of cases it’s diagnosed.
late with either regional lymph node spread or distant metastases.

And we know that when HTC is diagnosed late, survival goes down.

So five year relative survival and localized disease is 36.1% and overall five year relative survival is about 21. Percent.

We’ve moved the needle a little. It was about 18% in the last big sear.

Cohort that they looked at.

So how do we identify opportunities for directed education and outreach?

This is work that’s essentially a
it’s a mentorship of Doctor Strauss and Tabasco with Doctor Mezzacappa, one of our fellows. I’m looking at tumor registry and US Census data specific to Connecticut and we’re working with the Department of Public health in Connecticut. So this is geolocalization or hotspotting. And this approach we took to really kind of see where our case is most dense in the state and then what are some of the associations to the case rate and the stage diagnosis. And interestingly, we found not only this wide variation in cumulative incidence of HCC by ZIP code,
but also strong associations between Community level, poverty and education and the HTC case density. So really you could do this anywhere in the country. That I’ve taken you kind of from global to local, and I’m sure that Doctor Shaw, Sebasco and Doctor Mezzacappa will think about interventions in the community that we can actually improve our outreach and surveillance. So getting back to this conundrum with ultrasound,
so ultrasound is what we use in the present state for HCC surveillance, but we know that it lacks sensitivity for early stage detection and this has always been a problem. And it's also a problem of geography. In Europe, usually physicians do the ultrasound. The ultrasound body habitus is very different geographically. We have pretty large body habitus. And generally what you can see here is that while ultrasound may be OK for diagnosis at any stage. It’s really pretty poor for
00:12:50.190 --> 00:12:51.574 diagnosis at early stage.

00:12:51.580 --> 00:12:53.380 And no matter what stage you’re looking at,

00:12:53.380 --> 00:12:55.420 MRI really is the gold standard.

00:12:55.420 --> 00:12:57.016 The question is can you use

00:12:57.016 --> 00:12:58.679 something like an MRI to screen?

00:12:58.680 --> 00:13:01.518 And that’s sort of a question

00:13:01.518 --> 00:13:02.937 that begs asking,

00:13:02.940 --> 00:13:05.676 so can we move the needle on early
detection so we can do ultrasound, CT or Mr.

00:13:05.676 --> 00:13:08.753 These are the pros and cons.

00:13:08.753 --> 00:13:10.319 You know,

00:13:10.320 --> 00:13:13.812 clearly we can look at things like


00:13:16.080 --> 00:13:18.642 So for example in Europe.

00:13:18.642 --> 00:13:20.797 They use contrast enhanced ultrasound.
I don’t think that’s ever going to really take off here in the states for many reasons like lung cancer where you can use low dose chest CT for example, could you do low dose liver CT? Probably not because of the kind of resolution that you need to see liver cancer. But abbreviated MRI with shorter imaging times actually may be promising. With abbreviated MRI you can get a person on and off the table. In about 10-15 minutes. So this is something that we want to study.
And I think the VA is really the perfect place to study it. So cirrhosis is highly prevalent and MRI is really readily available at the VA and cirrhosis is quite common in the VA. The reasons for that is we have a 5 fold higher incidence of hepatitis C, which again is mostly now cured. We have very high prevalence of alcohol use disorder and very high prevalence of metabolic comorbidities. In addition, we have an aging population. And as you all know, cancer is a disease of aging. So it’s really the right mix of patients.
We are the largest healthcare provider for liver disease in the nation and we’re a closed system that can really look at our own metrics. So our electronic health record has been curated for research by the corporate data warehouse where we can really have wonderful, very rich data that spans 20 years. We also have operational sort of on the patient facing side, population health dashboards to identify patients in need of surveillance. We have clinical reminders that alert primary care providers to perform HC surveillance and we’ve made a lot of
NOTE Confidence: 0.874609802
00:15:01.898 --> 00:15:03.150 innovations with care coordination
NOTE Confidence: 0.874609802
00:15:03.205 --> 00:15:04.850 and navigation with online tracking
NOTE Confidence: 0.874609802
00:15:04.850 --> 00:15:07.199 tools that help us follow the patient
NOTE Confidence: 0.874609802
00:15:07.199 --> 00:15:08.814 through the continuum of care.
NOTE Confidence: 0.874609802
00:15:08.820 --> 00:15:09.466 And again,
NOTE Confidence: 0.874609802
00:15:09.466 --> 00:15:11.404 MRI is really readily available and
NOTE Confidence: 0.874609802
00:15:11.404 --> 00:15:13.382 we don’t have to prior authorize
NOTE Confidence: 0.874609802
00:15:13.382 --> 00:15:14.646 anything in the VA.
NOTE Confidence: 0.874609802
00:15:14.650 --> 00:15:15.800 Not nice.
NOTE Confidence: 0.874609802
00:15:15.800 --> 00:15:21.590 So so we can do this study in the VA.
NOTE Confidence: 0.874609802
00:15:21.590 --> 00:15:23.949 So the question is will earlier detection
NOTE Confidence: 0.874609802
00:15:23.949 --> 00:15:25.692 with abbreviated MRI actually result
NOTE Confidence: 0.874609802
00:15:25.692 --> 00:15:27.714 in a cancer related mortality benefit
NOTE Confidence: 0.874609802
00:15:27.714 --> 00:15:29.965 and this is what we want to find out.
NOTE Confidence: 0.874609802
00:15:29.970 --> 00:15:32.091 So our study called the premium study
NOTE Confidence: 0.874609802
which I’ll get to is a VA cooperative studies program funded study.

So the CSP actually funds very large scale trials only when they’re super convinced that we’re going to be asking fundamental questions that could change practice and they provide a dedicated coordinating Center for handling the trial across many centers. And we actually designed a study with a non screening arm which took a lot of convincing because gastroenterologists and hepatologists consider a non screening arm unethical and actually many other trials have tried this in patients simply wouldn’t enroll.
So the other issue is that we really do think that ultrasound is at this point insensitive. Enough that it’s actually not a bad comparator, since it’s standard of care anyway. So this is the study. It’s called preventing liver cancer mortality through imaging with ultrasound versus MRI. And it’s a randomized controlled trial of standard of care. Ultrasound plus AFP versus abbreviated MRI plus AFP every six months in patients with cirrhosis.
who have a high risk of HCC.
And some might say, well, geez, why are you starting there?
You know, there’s so many people who have so many variable risks,
why are you starting there?
And I think we have to start here because surveillance even in cirrhosis has poor uptake.
Poor uptake and a lot of debate still around it outside of the liver world.
So I think this is the right population.
This is the abbreviated MRI protocol if any of you are interested.
It really has all the sequences to diagnose HCC and the room time as
I said is about 10 to 15 minutes.

So we’re essentially taking a diagnostic exam, shortening it, still keeping the diagnostic sequences and using it as a screening exam.

Our primary outcome is cumulative HTC related mortality.

The study and which is your age for the surveillance portion and we’re powered to detect a reduction in HCC related mortality of 35%.

Of course, we’re going to be following any incident HCC through the life of the study as well.

So our study setting is 47
VA medical centers with high numbers of cirrhosis patients. According to those population health dashboards, they have to have adequate MRI capacity and access to a multidisciplinary liver tumor board for state-of-the-art treatment of HCC, which is a tall order. It’s one thing to diagnose a bunch of HCC, but if you’re not treating it correctly, that would really influence the study. So every center has to agree that they will send their patient to a tumor board and that they have access to care. The VA is very serious about trying to
enroll veterans all over the country.

So they have these network of dedicated enrollment sites that we’re working with and giving priority to the study.

Our total sample size is 4700 patients,

per arm and the duration is 9 years and it’s eight years in the surveillance and then nine years for data analytics.

And what’s interesting here is if you think about the burden to each center, we’re basically asking them to enroll about 100 patients over the enrollment period.
00:18:39.448 --> 00:18:41.806 be performing 100 extra abbreviated MRI.
NOTE Confidence: 0.811957548
00:18:41.810 --> 00:18:42.458 So you know,
NOTE Confidence: 0.811957548
00:18:42.458 --> 00:18:43.754 those people would have had an ultrasound every six months.
NOTE Confidence: 0.811957548
00:18:43.754 --> 00:18:44.688 They’re getting an abbreviated MRI.
NOTE Confidence: 0.811957548
00:18:44.690 --> 00:18:46.410 It’s not a huge ask.
NOTE Confidence: 0.811957548
00:18:46.410 --> 00:18:47.730 It’s actually fairly tenable for a larger center that has a functioning MRI.
NOTE Confidence: 0.811957548
00:18:47.730 --> 00:18:50.682 then everybody is you know in a surveillance pattern through year eight and then we analyze the data.
NOTE Confidence: 0.811957548
00:18:50.682 --> 00:18:54.298 And this is just a schematic of our
hypothesis and the difference between
abbreviated MRI and ultrasound.
So we hope that we're going
to detect cancer at
earlier stages, offer more curative therapy,
reduce HC related mortality
and if this is true,
then abbreviated MRI will be widely adopted,
MRI's are becoming cheaper.
So the hope is that this study will also
dovetail with technological advances
that make MRI within reach for patients.
And again you can see that
we're really hoping to.
Capitalize on the sensitivity of MRI.
So we will have a large bio and image repository. So we're going to be collecting blood every six months from patients when they come in for their imaging. That's going to be shipped to the A central biorepository for processing. We're collecting all the digital files for ultrasound abbreviated MRI. And so there are many possibilities for collaboration on biomarkers, both blood and imaging. And imaging is actually very important. There may be much that we learn from MRI's that has nothing to do with. Answer and the CSP is actually
00:20:11.024 --> 00:20:13.333 really nice at encouraging spin-off

00:20:13.333 --> 00:20:15.808 studies and in collaborating with

00:20:15.808 --> 00:20:18.780 other centers like NIH for example.

00:20:18.780 --> 00:20:21.180 So I talked about a biorepository.

00:20:21.180 --> 00:20:23.804 I think one of the biggest questions that

00:20:23.804 --> 00:20:25.896 the reviewers had for this grant was,

00:20:25.900 --> 00:20:26.560 well, hey,

00:20:26.560 --> 00:20:30.160 you can just screen for HTC,

00:20:30.160 --> 00:20:30.670 you know,

00:20:32.455 --> 00:20:33.779 it is a real threat.

00:20:33.780 --> 00:20:35.334 I don’t think it’s necessarily going to

00:20:35.334 --> 00:20:37.117 come to pass in the life of the study,

00:20:37.120 --> 00:20:39.388 but it is something that we felt
that a biorepository would be very useful to validate in a pretty heterogeneous population. And one can argue, well, the VA how heterogeneous is it? It’s a bunch of. Then, but the truth is, is that it’s actually quite heterogeneous in terms of ethnicity and background. So you can see here the present state of biomarker development development for early detection. There are four FDA approved biomarkers on this list here there’s AFP, AFP, L3, DCP and GALAD and their DRN
00:21:09.990 --> 00:21:11.490 phase of validation.
00:21:11.490 --> 00:21:13.289 So really AFP is hit prime time.
00:21:13.290 --> 00:21:15.390 I don’t think many of us use
00:21:15.390 --> 00:21:18.030 FPL 3 DCP or Gallatin practice, 
00:21:18.030 --> 00:21:18.986 but you can see.
00:21:18.986 --> 00:21:20.420 As you go down this list, 
00:21:20.420 --> 00:21:22.448 you’re starting to have multiple different 
00:21:22.448 --> 00:21:24.380 factors play into your algorithm. 
00:21:24.380 --> 00:21:26.428 So you’re you’re never going to find a 
00:21:26.428 --> 00:21:28.560 Holy Grail in HC of like 1 great protein, 
00:21:28.560 --> 00:21:29.271 one great marker. 
00:21:29.271 --> 00:21:30.930 It’s always going to be a mix 
00:21:30.988 --> 00:21:31.999 of different things, 
00:21:32.000 --> 00:21:35.260 clinical you know proteins etcetera. 
00:21:35.260 --> 00:21:37.936 So we’re getting much more into
sort of this algorithmic type approach to biomarker development.

Liquid biopsy, I think has been very encouraging.

In other cancers, it’s certainly encouraging an HTC, but it requires cross validation and better precision.

I would say that detecting early HCC is difficult actually. Where these biomarkers may be most important is in detecting recurrence, Umm.

So there’s a lot of work going on here. But I think for early detection, liquid biopsy isn’t yet ready for prime time. There’s a lot of things that are
very intriguing in liquid biopsy.
So it’s not.
Just circulating tumor cells,
it’s things like extracellular vesicles,
you know, circulating free DNA and methylated DNA.
So there’s a lot to learn here and a lot of platforms on which we can kind of look at different things from the blood that we collect.
So even with the best of intentions of trying to think about different populations, I can bring you down to the microscopic level and tell you that not only are our populations heterogeneous in terms...
of their ideology of liver disease, but the cancer itself is really heterogeneous. And there can be intratumoral heterogeneity, intratumoral heterogeneity. And so this actually becomes very complicated. And all of this is HC under the microscope. So you can see just how different some of these patterns. Yeah. So again, there’s intratumoral heterogeneity, intratumoral heterogeneity and this is really, you know, obviously interpatient heterogeneity, which I’ve discussed.
But then there’s a lot going on in terms of components of tumor heterogeneity in the liver. So the liver is a complicated organ where there’s a lot of innate immune suppression because actually the liver is what screens for foreign pathogens in your diet, right, and all the things that you’re seeing. So these cancers grow up in a fairly immune suppressed environment. So it’s a little bit different than the milieu of other organs. So there really is a lot to consider in terms of how to study this.
And teasing out oncogenic pathways from the pathways that are already upregulated from hepatic injury and repair is very complex. And I think we all like to think linearly, but it doesn’t really work here. So these are all the things that are associated with the paddock inflammation and fibrosis, some of them individually, some of them synergistically, some of them lumped together like metabolic, obesity, Nash and diabetes, which are all interrelated. And we like to think that all of these start this cascade that goes stepwise
from inflammation and fibrosis to advanced.

Fibrosis and cirrhosis to HCC, but it really doesn’t happen that way.

And we know that 20 to 30% of HTC and hepatitis B NAFLD and HIV arises in the absence of cirrhosis.

So we can’t really, although it’s very tempting, we can’t really think linearly here.

We have to think about different hits when in the lifetime these hits are happening.

what are the exposures, the persons involved with, etcetera.

So there’s a lot really to consider and I
think these stepwise schematics are great if you’re learning about the disease. So once you’ve learned about their disease, you realize just how complicated it is. So one of the things we’re looking at in the VA and this again work in the vocal cohort, which is a big virtual cohort of 130,000 patients with cirrhosis. And the VA over these past 20 years is some of the effects of blood glucose control and some hypothesis and we actually found quite antithetically that sustained blood glucose
00:25:09.298 --> 00:25:12.560 control actually increases your risk for HTC.
00:25:12.560 --> 00:25:14.294 Why is that? It’s because of the Tropic effective insulin.
00:25:14.294 --> 00:25:18.050 So we have to actually look at the pharmacoepidemiology of these patients when they were started on insulin,
00:25:18.050 --> 00:25:21.505 when in the course of their diabetes and their liver disease they were started on insulin, what other drugs they received etcetera.
00:25:21.510 --> 00:25:23.028 when in the course of their diabetes and their liver disease
00:25:23.028 --> 00:25:24.389 diabetes and their liver disease
00:25:24.389 --> 00:25:25.889 they were started on insulin, what other drugs they received etcetera.
00:25:25.890 --> 00:25:28.890 what other drugs they received etcetera.
00:25:28.890 --> 00:25:31.226 So this is really just to show you the robustness of the associations
00:25:31.226 --> 00:25:32.691 the robustness of the associations
00:25:32.691 --> 00:25:34.609 you can look at in the VA, but that you can’t stop there.
00:25:34.610 --> 00:25:36.230 but that you can’t stop there.
00:25:36.230 --> 00:25:37.796 Actually there’s a whole lot more
that has to be done both in terms
of looking at the richness of
the pharmaco epidemiological data
but also then mechanistically.
So this is really nice.
To be able to kind of take a really
like 30,000 foot view and say what
are all the things that now we need to
study based on what we found is what
we didn’t expect quite a paradox here.
So HTC is clinically complicated
because it’s unique among cancers.
And this is where I think
oncologists sometimes say, oh,
00:26:06.400 --> 00:26:07.216 be unique, right.
00:26:07.216 --> 00:26:08.576 There’s nothing unique about this,
00:26:08.580 --> 00:26:10.780 but it really is unique.
00:26:10.780 --> 00:26:14.791 and cirrhosis leads to multifocal
00:26:14.791 --> 00:26:16.795 liver cancer because of the field
00:26:16.795 --> 00:26:19.080 effect and very high recurrence rates.
00:26:19.080 --> 00:26:20.885 It also really has complicated
00:26:20.885 --> 00:26:23.040 treatment and trial design and it
00:26:23.040 --> 00:26:25.028 is a a cancer that’s something of
00:26:25.028 --> 00:26:26.753 an anathema to oncologist because
00:26:26.753 --> 00:26:28.209 you guys like tissue.
00:26:28.210 --> 00:26:30.426 And we can diagnose this by imaging alone.
00:26:30.430 --> 00:26:31.970 And actually that’s where I
00:26:31.970 --> 00:26:33.510 think our field has misstepped.
I think we actually put ourselves way behind without getting biopsies for so many years.

It is the only solid organ malignancy for which transplantation offers a cure, which puts the onus on us to make sure that we’re sending the right people for transplant.

But surgeons love to push the envelope. They should push the envelope and we’re really beginning to push the envelope, meaning that people who we thought had disease way outside bounds are having remarkable complete responses on immunotherapies and coming back to transplant,
which is very weird and very frightening for many of us. But their early responses look really good. So I think we’re going to see a lot of stage migration with the newer therapies and we’re going to have to be very, very careful in how we treat these people. And I think the adage of just because you can do it doesn’t mean you should do it is something we have to take very seriously as as this landscape changes in terms of treatment. So the treatment of HCC up until now has followed a very linear pathway from early to advanced disease.
So hepatology surgery, surgical oncology and transplant surgery and interventional radiology have really dominated early stage disease. And oncology is usually consulted only in diffuse infiltrative disease or in intermediate stage disease or in advanced disease with vascular invasion or extrahepatic Mets. And that’s really unfortunate for the oncologist because sometimes they’re really referred to you too late and they’re too sick. The treatment and had you brought your expertise to the table earlier on, it probably would have
actually been really good. So I think oncology now feels very much welcome at the table because we do have so many new treatments. But also the lack of that expertise for so long because we really didn’t have good systemic therapies, I think really detracted from our development as a field. So the advent of new therapies is definitely changing this paradigm, not only the timing of specialty involvement. But also the types of specialists involved, for example, SBRT now has a place in the
arsenal for HCC management.

So this is not for you to memorize, but the staging classification that we use called the BCLC staging classification. And the things that I just want to draw your attention to is that really we have to think about the patient and their functional status first in terms of their liver function. So this is really what drives our initial decision making before we even begin to count tumor. Or think about tumor burden and then tumor burden is actually looked at across, you know very early, early, intermediate and advanced stages.
And then we have treatments ascribed to those different stages with an expected survival, which I have to say has gone up significantly in the last 10 years. You know, essentially it used to be 3 months for advanced stage and now we’re looking at, you know, over two years, over 2.5 years for taste. I mean, these are quite big differences than 10 years ago.

What’s new about this classification is everything below this blue bar,
so essentially before I go below the blue bar.

I just want to say that they’ve now separated out intermediate stage disease because we know that diffuse infiltrative HCC is a different actor, especially when it’s by low bar,

you really can’t approach it locally. But we’ve now put in successful downstaging again moving back towards a curative or transplant effort.

And then the stage migration is a theme that’s really being played out both by surgical oncologists and transplant surgeons.

And then we have now up to three.
Kinds of systemic therapy when we only had one line for 10 years. So in the last five years, we've seen a lot of change. And that's really why multidisciplinary care is essential. So we really have to define our endpoints. So we want to improve survival. Everybody wants to improve survival, but survival is relative to the liver disease. So you really don’t want to offer a treatment that’s going to hasten somebody’s death from liver failure. And that is a very,
very tough decision that requires a lot of thought.

You really need to know your patients, you need to know their markers, you need to know them well.

Proper risk assessment and obviously proper patient selection is key to any surgeon. You know, there are standards that have to be set and there’s, as I’ve mentioned, a lot of Gray areas, but there’s also a lot of variations among disciplines. For example, surgical oncologists approach surgery...
very differently than transplant surgeons.  And there's variations among programs and regions.  And especially when it comes to liver transplantation, there's significant variation.  So our job as a group of people who take care of these patients in a multidisciplinary way is to identify the optimal candidates for treatment.  We consider them across the continuum, weavering patients back to tumor board all the time.  And I would argue that every single
recurrence and every single new tumor has to be brought to tumor board because you will forget that patient and you will miss their opportunity for something that could really prolong your life. So tumor board for liver cancer I think is absolutely necessary. You can’t take care of these patients alone. You don’t want the onus of all that decision making falling on one person. And this graphic is from a paper written by Doctor Jaffe here at Yale really kind of describing this playbook. essentially the hepatologist is quarterback.
Usually these folks come through us and then we bring them to tumor board. But there are a lot of different referral lines and we’ve seen people coming through oncology, coming through interventional radiology. The most important thing is that you discuss that patient before you treat them and that really should be the norm because there are always new ideas and if you don’t discuss, you won’t think about, you know, what could be a potential, you know, better therapy.
Remember that tumor boards actually serve a lot of purposes. They are accredited. They have to have mandatory attendance from certain disciplines. They have a liaison to the tumor registrar so they can actually pick up cases and report them early. They provide an objective forum for discussion and that they really should be that, an objective form for discussion where everybody, everybody’s opinion matters. They should foster trial enrollment and they do.
There are many studies that have shown that and they really help to set institutional guidelines in gray areas, of which we have many. They're also a really important thing for trainees. So the one thing I loved most as a medical student was multidisciplinary team reward. So it's no, you know, strange thing that I ended up running tumor boards. So our tumor boards in the VA are regional. So I run a big Southern New England regional tumor board that takes care of Vermont and Providence,
Also Rhode Island, Vermont, Massachusetts, Connecticut. This is actually a study of about 4000 patients across the VA. And what we found in this study was that seeing a hepatologist actually was associated with a 30% mortality reduction, but it wasn’t associated with higher odds of receiving active therapy. So what does that mean? That means we’re actually carefully deciding who can get therapy and who should not get therapy because...
we know that palliative care in hepatology can prolong life in liver cancer and in in stage liver disease. It’s knowing who’s the right person for that palliative therapy versus who’s the right person to get treatment. And very encouragingly to me because tumor board is a labor of love and very labor intensive, multidisciplinary tumor boards also were associated with lower mortality. So this study was very heartening. So we have many options for local regional therapy and early and intermediate stage disease, Umm.
So this is the part of the BCLC classification from very early to intermediate stage.

And we have liver resection and liver transplantation not for the faint of heart.

You need to have really good liver function for a liver resection.

Liver transplantation is wonderful because it cures the underlying cirrhosis and the liver cancer, but it’s not for everyone and there are very strict criteria for who can and can’t get transplanted.

Local regional therapies abound. And ablation now can be given thermally, chemically and also with SBRT.
So there’s emerging data to suggest that SBRT and small lesions does have ablative and curative properties for palliative intent. So this is moving more towards intermediate stage B disease. There are transarterial therapies, chemoembolization and etrem or why 90 treatment and then SBRT. So these therapies are supposed to prolong. By about 2 1/2 years, which is pretty considerable and people have pretty good quality of life with these therapies. The one thing is that these transarterial
therapies do take out a penumbra of functioning liver and so you really have to think about their liver function. Same with ablation, but less so. Ablation is usually pretty targeted. So this actually is data that’s going to be published as part of the ASLD guide guidance for HCC. And what I can tell you is that in considering this guidance, the way that we interpret CT’s and MRI’s in patients with cirrhosis is very standard because the reason that we can make this diagnosis without a biopsy is that these tumors look
very characteristic on imaging.
And this has guided our field for a long time and for a long time we actually argued against doing biopsy because. They feared tumor seeding especially in the transplant patient.
But really tumor seeding is very rare and nowadays we have better technology and the way we do biopsies and so it’s quite rare and good hands. And So what we’ve tried to do is explain that biopsy actually may be very important, especially when you’re not entirely certain because some therapies can be
offered and you may lose your window. 

So now we actually recommend biopsy and lyrids 4, probable HCC, lyrids 5, you certainly can. Biopsy when they’re deaf, quote, definitely HTC and lyrids malignancy means you can’t really determine if it’s an HTC. So biopsy was always the norm there. And then if you have tumor in vain, you may be able to biopsy to do Umm, you know, testing, for example, a tumor profiling. So I think we’d like to see more and
more biopsies being done and being done rationally across the continuum of care, but this guidance is at least an opening to try to get people to think about it. So now the choice of systemic therapies, these are people who have either extensive by lobar liver involvement, they’re called. extensive by lobar liver involvement, they’re called. Intermediate stage or advanced stage when they have tumor that goes outside the liver or tumor that’s in the lymph nodes or veins. So we have a lot of new therapies and here you can see trials that have been,
these are FDA approved drugs,

their superiority trials,

non inferiority trials in phase two trials.

I'm not going to go into this

because I think this audience

understands how these agents work,

but what I can tell you is that we have.

Had an onslaught of agents and

really a very short period of time.

So just like we used to get dizzy when

we had all the new hep C therapies.

And I used to say to myself, oh,

thank God, I'm not a virologist now.

I'm like, oh gosh, thank God,

I'm not an oncologist,

but it's really not true.
I think we actually, we actually understand these agents very well. And I think those of us who do immune therapies like for example, inflammatory bowel disease or transplant, we’re actually pretty savvy with using immune therapies, so. We understand this language, we understand the side effect profiles and we’re very happy that there are a lot of different agents.
and we’re not really sure yet. So you can see that just in the last five years, we’ve had eight new sort of regimens come to market. What I do want to show on this slide is that in the sharp trial, the overall survival in that population in the placebo arm was 7.9 months and the sorafenib arm was 10.7 months. So that’s median overall survival. And flash forward now to 2022 and you can see that for all the verses sorafenib trials. The survival is actually quite a bit longer. We’re looking at about anywhere...
00:38:55.940 --> 00:38:57.350 from 12 to 14 months.
00:38:57.350 --> 00:38:59.210 So we’ve definitely moved the
00:38:59.210 --> 00:39:01.070 needle on probably patient selection
00:39:01.132 --> 00:39:02.597 and other things you know,
00:39:02.600 --> 00:39:04.945 getting used to using these drugs etcetera.
00:39:04.950 --> 00:39:08.086 So I think what you’ve seen is actually.
00:39:08.090 --> 00:39:09.506 The field and the Natural History
00:39:09.506 --> 00:39:11.405 of the field moving as well and you
00:39:11.405 --> 00:39:12.767 can’t really take that for granted.
00:39:12.770 --> 00:39:13.880 I think it’s an important thing
00:39:13.880 --> 00:39:15.040 that people don’t talk about much,
00:39:15.040 --> 00:39:17.230 but getting used to using TIs in
00:39:17.230 --> 00:39:19.005 patients with liver disease was
00:39:19.005 --> 00:39:20.240 pretty difficult. All right.
00:39:20.240 --> 00:39:21.540 So here’s our current paradigm.
It’s based on clinical characteristics. So we look at advanced stage HCC, either BCLC or intermediate stage B with, you know, those caveats as I mentioned. We want to think about contraindications for immune therapy, which is something we didn’t think about until these drugs came to market. So what kind of autoimmune disorders does a patient have? Might they be going for liver transplant? Should we check with the liver transplant Center if there if they would be OK with transplanting a person who received an immune checkpoint inhibitor and then we actually have to think about other things.
So right now the first line choice is atezolizumab and bevacizumab. Bevacizumab is a VEGF inhibitor with a higher risk of bleeding. And so in the in brave 150 trial which is what brought this to market, they did an EGD. Within six months of the patients going on this regimen, not a great real-world thing. It’s really hard to get all these people in for an EGD. The problem is, what if they actually find varices and there was no stigmata of bleeding?
Then what do we do?
And actually, the trial said that they were treated according to institutional norms, which is a big gray area.

But my thought is if they don’t have stigmata of bleeding, try the drug, make sure you tell the person there’s a higher risk of bleeding and, you know, don’t bother banding them and putting off their therapy for months. That’s kind of ridiculous. So there’s now a lot of real world OHS that came out of these trials as as always happens,
but we have to think about these things.

So Ateso, Bev is the first line choice for our patients if they can have these drugs. Tremelimumab and durvalumab just came on the market and then there are a lot of people who can’t have immune checkpoint inhibitors and they can still get TI. The areas that are sort of dashed and Gray are sort of entirely data free zones. So these areas here if you can. My cursor, which I don't think you can. So what happens if they got an immune
checkpoint inhibitor in for in frontline, you know, can they go back to a TKI. So these are things we're not entirely sure of. So there's a lot of room to study these things. What's important is what we're missing, which is that all of these trials are done in child Pugh a patients. So these are well compensated patients. They look fine. They don't have any complications of their liver disease and actually a lot of our patients have complications of liver disease when they're diagnosed with their HCC.
So we want agents that can help with Child Pugh B patients. These are patients who you know may have a low albumin. They may have, you know, prolonged INR, they may have trace societies that’s controlled with diuretics, for example. So as part of our recommendations we really think that well selected child pubby patients should be offered either TI’s which have been studied in them or single agent anti PD one or anti PD L 1 immune checkpoint inhibitors.
combination therapies really haven’t been looked at in these patients.

So I think we have to treat those patients carefully.

So I think one of the problems that we have with understanding the data around immune checkpoint inhibitors is how variable the predictability of responses.

The. Predictability of responses.

So these are people who had a partial response and a goal triangle and you can see it’s all over the map and there are people who have really, really long ongoing responses until they then develop progressive disease.

So all of the arrows are people who were
still alive after 72 months towards that end.

And then all of the, Umm, you know,

blocks where they end show where

they progressed and and passed away.

But I mean,

I think that the interesting thing here is.

Well, who are these people who can

have this 72 month long response?

So this that data was from the keynote

trial which was pembrolizumab

after progression of disease with

sorafenib and I think this is what

really got a lot of us thinking.

But more recent data that comes

out of the in brave 150 At’s above
trial really shows us the landscape of the immune profiles of these patients and the fact that the ratio of T regulatory to effector T cells really matters in terms of survival, especially with immune checkpoint inhibitors.

So I think this is definitely getting towards the more personalized approach and how to figure out who should get these drugs, some of the interesting things that have been published lately. And the GI world or liver world is this paper that looks at you know essentially frontline PD1 inhibition.
00:43:52.128 --> 00:43:54.949 or PD1 treatment compared to receiving PD1 as a second line or third line.

00:43:57.990 --> 00:44:00.006 So here you can see that if you start with PD one and first line,
00:44:00.006 --> 00:44:01.890 it's more likely that you're going to have a complete remission or a partial response as opposed to if you start in second line and third line when you're more likely to have stable disease or progression of disease.

00:44:06.879 --> 00:44:08.735 you start in second line and third line when you're more likely to have stable disease or progression of disease.

00:44:12.670 --> 00:44:14.315 So this was a pretty small trial and there were.

00:44:15.020 --> 00:44:17.852 Issues in terms of the timing of biopsies and the timing of duration of disease.

00:44:20.810 --> 00:44:23.239 But what you can see is that
clearly over overall survival
and progression free survival and
frontline anti PD one therapy for HCC is really quite impressive.
What is even more interesting about this paper which just came out was really that they were able to take and develop sort of a signature and Interferon antigen presenting signature they called it if interferon AP they called it if interferon AP essentially and what you can see is that people who had the signature obviously they had increased CD4 memory activated T cells and M1 macrophages and plasma cells in the
00:45:02.042 --> 00:45:04.384 tumor microenvironment. They responded.

00:45:04.384 --> 00:45:06.494 The non responders really had

00:45:06.494 --> 00:45:09.044 significantly higher you know T regulatory

00:45:09.044 --> 00:45:11.079 cells in the tumor microenvironment.

00:45:11.080 --> 00:45:13.696 So I think we're getting more and more

00:45:13.696 --> 00:45:15.190 into personalization but obviously.

00:45:15.190 --> 00:45:16.996 These trials had big data repositories

00:45:16.996 --> 00:45:18.750 and they're just still reporting,

00:45:18.750 --> 00:45:20.654 so I think the next couple of

00:45:20.654 --> 00:45:22.610 years will be very interesting.

00:45:22.610 --> 00:45:24.248 So I think bottom line is we

00:45:24.248 --> 00:45:25.332 need to collectively strive

00:45:25.332 --> 00:45:26.668 for a personalized approach,

00:45:26.670 --> 00:45:28.235 whether we're looking at population

00:45:28.235 --> 00:45:30.749 health or looking at the patients biology.
And so this is kind of where we were. I think we’re moving more towards the tailored approach. But you can see when you kind of throw all of these populations together, give them a treatment, you get a 20% response and that’s great and we can show that and that’s wonderful. But the real question is who are these people who are going to respond or not going to respond and how can we actually properly categorize them so that they can get the treatment that they need and this is really what we’re doing you know all throughout our clinical and research lives.
So what are the most pressing clinical and research related needs? I think access to care for prevention and screening is #1. A lot of liver disease actually is something that is modifiable early diagnosis. So imaging of course liquid biopsy tissue we need clinical blood based imaging we need clinical blood based imaging and tissue biomarkers for detection, prognosis and. Response to treatment, I don’t think it’s going to be one or the other. I think it’s going to be all of them. And the mechanisms of pathogenesis...
and tumor behavior really are still in many ways unknown.

We’re working on it, but we have a lot of questions. The order and timing of treatments and sequential classification is really important. So revised tumor staging, we really have to start getting into it and we have to do it for stage migration and stage shift and we really need to deliver value based care. These patients need to be taken care of in a multidisciplinary environment where they really feel that the whole team is there.
for them and that they’re the Most Valuable Player on the team.

So my key takeaways,

the epidemiology of HC is shifting.

Fatty liver disease is a big new kid on the block, no pun intended.

That was terrible. I’m sorry.

We need, we need to embrace complexity, technology and team based care and science to offer our patients the best possible outcome.

So really when we break down silos across care and science, we actually do the best science. They really need a
00:47:26.600 --> 00:47:27.885 It’s the mainstay for complex decision making and I think people always feel better when they’re part of a collective and really come up with a good plan of care.

00:47:33.920 --> 00:47:35.660 We should really push the envelope. It’s important to push the envelope, most ideally in a clinical trial setting. And the surge in large scale observational and omic data should help inform large prospective trials as well as all the analytical platforms we have for these data.

00:47:53.050 --> 00:47:55.340 And systemic therapy options continue to grow for advanced HCC patients.
But now is the time that we should stop looking at that 20% response and actually figuring out who we should treat when and with what. We definitely need a better understanding of when to introduce systemic therapies and there are 150 ongoing clinical trials that are going to reshape the field. In terms of adjuvant, neoadjuvant, the game is just beginning. So I really want to thank a lot of people, really most importantly Amy Justice, who really mentored me for the virtual cohort at the VA and through a lot of the work we’ve been doing on HIV associated HC.
Dave Kaplan, who’s my Co, 

Pi in the vocal study, 

Georgianna, Who’s my Co 

Chair of the premium trial, 

Mario who’s mentored me for probably more 

years than he’d like to think about, 

Catherine Mezzacappa provided me with this. 

Sides of her preliminary work and she 

just received a liver pilot grant, 

which is wonderful for her Rajni meta, 

from the rapid case ascertainment 

resource for the Cancer Center, 

who’s really been my right hand now for 

well over a decade and many, many more, 

but most importantly my patients. 

So thank you.
Yes.
The light.
So one of the things that I think about is we do see this, as you point out, looming.
Epidemic with Don alcohol.
It is exciting to think about surveillance and seed interventions in the.
Anti violence phase,
but we actually have an enormous capacity for risk reduction in fatty liver disease.
Do you have any interventions in the planning stages for that and need any prospective studies?
I don’t have studies of my own.

I can tell you that I’m pretty active with the American Liver Foundation.

That does a lot around educating the populace about all of these sort of lifestyle, you know, and preventative measures.

I think we have to start with our children and I really wish that there was a way that we could actually have pediatricians and hepatologists, you know, kind of come together and maybe maybe.

Maybe it’s the best thing for pediatric hepatologists to figure out how to educate children about food, food shortage, healthy eating, exercise.

So, you know, pharmaceuticals,
they’re sexy and there’s a lot of money.

And there’s really not so much money for preventive medicine and especially for these food deserts, which actually beg a much larger question of the social determinants of health.

It’s a huge, you know, bite to take off and chew.

I mean it troubles me that you know the disparity of resource put in One Direction versus the other.
00:50:58.480 --> 00:50:59.020 Question.
NOTE Confidence: 0.618677115
00:51:02.140 --> 00:51:03.766 I don't understand.
NOTE Confidence: 0.618677115
00:51:03.766 --> 00:51:08.490 What's your DNA? Endoscopies.
NOTE Confidence: 0.88699267
00:51:10.960 --> 00:51:14.188 So we yeah. Oh, sorry.
NOTE Confidence: 0.638228464857143
00:51:16.210 --> 00:51:21.470 If you can call back attention and
NOTE Confidence: 0.638228464857143
00:51:18.440 --> 00:51:21.470 you've got valuable. Doesn't need, right?
NOTE Confidence: 0.525612733333333
00:51:24.260 --> 00:51:26.549 So suppose that.
NOTE Confidence: 0.621648143333333
00:51:31.010 --> 00:51:33.068 Yes. Patient has
NOTE Confidence: 0.393635345
00:51:34.110 --> 00:51:35.340 significant potential.
NOTE Confidence: 0.867354756666667
00:51:37.810 --> 00:51:38.746 What are you going to do?
NOTE Confidence: 0.867354756666667
00:51:38.750 --> 00:51:40.442 Nothing, right? So you you
NOTE Confidence: 0.867354756666667
00:51:40.442 --> 00:51:42.020 did a meaningless test, right?
NOTE Confidence: 0.57213502625
00:51:43.560 --> 00:51:44.680 Just before the treatment,
NOTE Confidence: 0.57213502625
00:51:44.680 --> 00:51:45.800 which is not indicated,
NOTE Confidence: 0.57213502625
00:51:45.800 --> 00:51:47.690 is outside with the guy, right?
NOTE Confidence: 0.8547659975
00:51:49.810 --> 00:51:50.398 What do you do?
Right. So um. We do the endoscopy because I, I’m working on oncology at the VA, but it’s not they really want the endoscopy if there are no stigmata of bleeding, I do not band. And I say, hey look there’s portal hypertension here, there’s some variances, right, the patients on carvedilol and they’re like OK, at least you know, at least we know what we’re getting into. So the patient could bleed. I said the patient could bleed from gastritis like what’s you know.
In the next year or two is sort of more phase four kind of what’s the real world experience because I’m sure that in the VA system people are getting a Tiso Bev without a prior EGD because not all centers are big enough etcetera, etcetera. So, so we actually have some designs on doing that sort of study. Yeah, they’ve come to us, Mario, for the data. Yeah. Yes, Tommy? the uptake in atisa above has
really only been, you know, it had a slope of uptake 2122. O I’m not sure that I can answer that question. What I can say is we’re seeing much more advanced disease at presentation because people didn’t come in for imaging and that is really heartbreaking, So it’s that’s pretty awful.
But I don’t think I’ve, I’ve have enough experience over the FDA approval to say that there’s been any difference? Are you thinking just about immune regulation post COVID or? Hmm. OK. Right. Hmm. That’s an interesting thought. I mean, I can tell you our rates of alcoholic hepatitis are skyrocketing, and they’re skyrocketing among young people. So there is definitely a lot of psychological burden from the pandemic, so.
00:54:56.310 --> 00:54:59.118 OK. Sorry, I fell down on the job here.

00:54:59.120 --> 00:55:01.878 OK. So one of the questions was, as you mentioned, some oncologists are reluctant to use atisa Bev of smaller large varices or even hemorrhoids.

00:55:01.880 --> 00:55:04.448 reluctant to use atisa Bev of smaller

00:55:04.448 --> 00:55:07.322 large varices or even hemorrhoids.

00:55:07.322 --> 00:55:09.105 Any suggestions how to convince them to use this regimen without banding? So I mean,

00:55:09.105 --> 00:55:11.785 Any suggestions how to convince them to use

00:55:11.785 --> 00:55:14.304 this regimen without banding? So I mean,


00:55:16.307 --> 00:55:18.629 I think it’s really basically saying,

00:55:18.630 --> 00:55:19.750 you know, we’ve got this,

00:55:19.750 --> 00:55:21.628 if the person bleeds were here,

00:55:21.630 --> 00:55:22.878 they know how to reach us,

00:55:22.880 --> 00:55:24.440 we know how to reach them.

00:55:24.440 --> 00:55:27.296 You know, we’re available, if anything.

00:55:27.300 --> 00:55:27.768 Thumbs up.
You know, Yale is a center of excellence in terms of hepatology care.

So is West Haven.

We know how to ban people if they bleed.

I think it’s really honestly getting them used to using the combination and not seeing a lot of bleeding.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.

Laura Morrison asked, can you please share your latest innovations and Co management of these patients with palliative care at the VA.

And I think it’s just going to be tincture of time.
Our palliative care fellows always appreciate the different model at the VA that’s very lovely.

Thanks Laura.

So yes, we are Co localized with palliative care, so they come to our clinics. We have a clinical trial that’s enrolling patients and it’s a clustered randomized controlled trial of standard of care, palliative care intervention versus hepatology trained palliative care.

So our palliative care docs, we are randomized to the
palliative care intervention.
So it’s the standard of care palliative
care consultant and having them at the tumor board and in clinic is wonderful. So all of our end stage liver disease patients, all of our multifocal HTC’s, they all see palliative care from the get go. So it’s not like this awkward handoff where you’re like OK now you’re really sick and you need to see the palliative care doctor. It’s it’s from the beginning we say we work together. Palliative care is a layer of support. They’re here to really think.
about other things.
You may not be having any symptoms now,
but they’re going to help you get your logistics straightened out or they’re going to help you get help into the home if you need it, or they’re going to think about the things that really matter to you while we’re focusing on your organ here, we’re myopic in specialty care where we just focus on the organ that we’re thinking about and like rarely do we say, so you know,
what are your goals like?

What’s really important to you?

How do you want the next few months to unfold?

Because I think a lot of us are afraid of the Pandora’s box that’s going to open because then we actually may have to connect with another human being.

And palliative care is wonderful because they teach us like I have learned so much from palliative care, how to open a conversation, how to ask difficult questions, how to know when I’m over my head. So I would say that most of us at
the VA really know how to deliver, you know, primary palliative care. And we rely on palliative care for specialty palliative care, which is really. What their experts in and we're hoping that we can impart that kind of training nationally. So that's going to be the results of that study which is funded by PECORI and which is basically a multi center private NBA study that's at the PI's Victor Navarro out of Jefferson in Philadelphia. Thanks Laura.
00:58:06.280 --> 00:58:08.688 I think that's it. Any other questions?