OK, why don’t we? Oh, get started. We have a good number of people on the line now. Welcome to grand rounds. Today May 18th, 2021. We’re focusing on GI cancers today, challenges and opportunities and we’ll hear from two members of that newly formed center. It was actually the first official disease center that we formed, and it’s fitting that we have these two speakers. And what we’ll do is we’ll have each
00:00:35.778 --> 00:00:38.290 speak for 2025 minutes and then
00:00:38.290 --> 00:00:40.906 we’ll do some questions right after.
00:00:40.910 --> 00:00:43.675 So the first is Doctor Pan Kunz,
00:00:43.680 --> 00:00:46.050 who is associate professor of internal
medicine and medical oncology,
00:00:47.630 --> 00:00:50.367 and the director of the Center for
GI Cancers and the and the
00:00:50.367 --> 00:00:53.184 GI Medical Oncology.
00:00:53.184 --> 00:00:55.530 the Chief of GI Medical Oncology.
00:00:55.530 --> 00:00:58.690 And we’re really fortunate to have Pam here.
00:00:58.690 --> 00:01:01.448 She’s been here less than a year.
00:01:01.450 --> 00:01:03.804 She moved from Palo Alto, Atherton.
00:01:03.804 --> 00:01:06.422 And two New Haven during a very
tough year to travel.
00:01:06.422 --> 00:01:07.969 So we’re so happy you came Pam.
00:01:07.970 --> 00:01:10.574 So the first is Doctor Pan Kunz,
00:01:10.580 --> 00:01:12.340 She received her medical degree
from Dartmouth Medical School and Residency and Fellowship at Stanford.
She then state was at Stanford until she joined us in 2020 at Stanford.
She was the director of the Stanford Neuroendocrine Tumor Program, the leader of Endocrine Oncology Research Group and the Director of the Neuroendocrine Tumor Fellowship.
As you all probably know, she’s an international leader in the clinical care of patients with neuroendocrine tumors. We call those Nets and ETS and is advancing the field through clinical trials and translational research.
She's got a broad investigation or program and you're going to hear today about her, her plans, and what she's already initiated to really build her own program. But more importantly, the entire Geo program here at the Yale Cancer Center Smile Cancer Hospital, so Pam, thanks for being here today and I'm looking forward to your talk. Thank you, right? And right just give me a thumbs up but can you see my screen OK? OK, excellent good.
Well thank you everybody and where I thank you for that kind introduction. I’m very excited to share with you our GI cancer program. But before we jump in I just want you to save the date for a very exciting grand rounds in two weeks. See we’re having our first annual yield Center for GI cancers. Visiting lectureship with Doctor Marcia Cruz Korea. She is a professor of medicine and biochemistry and the director of the GI Oncology Program at the University of Puerto Rico. She has held leadership roles in ACR,
most recently the women in Cancer Research Committee and she was the chairperson for that. The focus of her research is understanding genetic and AP genetic pathways for colorectal cancer among Hispanic patients. So we’re very excited to host her in a couple of weeks. So I will be sharing the virtual podium today with Doctor, Mandar, Mazumdar and we are excited to share with you an overview of the program and some of the goals Mander will take on the scientific vision.
So I'd like to start off just by recognizing that this is an incredible team effort and what I will be talking about today really is the work of the entire team. It's been a pleasure to get to meet everybody, mostly by zoom over the last year, but we have really tremendous team members and have started also doing some recruiting. These are my disclosures, so I will take on providing you a background on GI cancers talking about this newly launched center and then I'll speak about our patient care,
education and clinical research initiatives and then I will pass the baton to Doctor Mazumdar. So first just a brief background on GI cancers and aspects that make up make our center unique. So if you try to count up all of the different primary sites in the GI system, there are at least 12. Depending on how you count them, and I think that poses both some challenges and some opportunities as we think about developing a center and really trying to address all of these different primary sites via all
of the main pillars of patient education, patient care, education, and research.

In terms of estimated new cancer cases, colon, rectal and pancreas are in the top 10 for both men and women. However, there is a larger proportion attributed to GI cancers or estimated deaths. In fact, 27% of estimated deaths in men or due to GI cancers school in pancreas, liver, and oesophageal and for women it’s about 21%.
We’ve also had a number of FDA approvals over the last 12 months. This is since May of 2020 in fact, just in the last six weeks we’ve had three new FDA approvals in the immunotherapy space for advanced Asafa Geo, GE Junction, and gastric cancers. You’ll see in those last three rows Pembroke Plus for permitting nivo plus floor permitting and Pembroke Plus tries to the map in floor permitting. So it’s been very exciting for us. GI cancers have also been in the news quite a bit in the last year, which I think has done a lot to raise
awareness, which is quite important. So Chadwick Boseman sadly died at a very young age of colorectal cancer. Ruth Bader Ginsburg died of metastatic pancreas cancer. We’ve also seen recommendations for the colon cancer screening age to drop to age 45, and this is on the basis of a draft recommendation from the United States President. For average risk, adults age 45 to 49 that they should start screening. This is not been put into practice just yet. So in terms of our center, I think Kevin best for this slide.
Many of you have seen this, but Roy and I are in a bit of a competition, so both of our centers have launched. We went. We just edged out the thoracic center, but it’s very exciting and there are 13 more centers yet to launch. These centers, I think, as many of you know, have a shared organizational structure with a leadership cabinet. There are common rules in all the disease centers. These include the director, and I will be serving that position.
00:06:46.898 --> 00:06:49.064 for our center patient care Services
NOTE Confidence: 0.810886
00:06:49.064 --> 00:06:50.989 Director Maureen Major Campos and
NOTE Confidence: 0.810886
00:06:50.989 --> 00:06:52.549 Operations and planning director.
NOTE Confidence: 0.810886
00:06:52.550 --> 00:06:55.490 Which is Kevin best?
NOTE Confidence: 0.810886
00:06:55.490 --> 00:06:57.338 I also have a scientific director,
NOTE Confidence: 0.810886
00:06:57.340 --> 00:06:58.572 doctor Mandel, Razum Dar,
NOTE Confidence: 0.810886
00:06:58.572 --> 00:07:00.420 which I’m very excited about it.
NOTE Confidence: 0.810886
00:07:00.420 --> 00:07:02.410 I’m currently serving an interim
NOTE Confidence: 0.810886
00:07:02.410 --> 00:07:04.400 role as the clinical director.
NOTE Confidence: 0.810886
00:07:04.400 --> 00:07:06.986 We also have the flexibility of
NOTE Confidence: 0.810886
00:07:06.986 --> 00:07:10.134 adding a number of ad hoc rules
NOTE Confidence: 0.810886
00:07:10.134 --> 00:07:11.910 specific to GI cancers.
NOTE Confidence: 0.810886
00:07:11.910 --> 00:07:14.710 We wanted all of the relevant stakeholders
NOTE Confidence: 0.810886
00:07:14.710 --> 00:07:18.536 to have a place in this leadership cabinet.
NOTE Confidence: 0.810886
00:07:18.540 --> 00:07:21.198 So these include Sir junk education,
NOTE Confidence: 0.810886
00:07:21.200 --> 00:07:23.410 cancer imaging, RAD ONC pathology,
and Network Director,
00:07:24.733 --> 00:07:26.056 biorepository advanced endoscopy
00:07:26.056 --> 00:07:26.938 and importantly,
00:07:26.940 --> 00:07:30.804 a liaison with the GI service line.
00:07:30.810 --> 00:07:32.980 You’ll see that that GI service line
00:07:32.980 --> 00:07:34.684 dotted line is really indicated
00:07:34.684 --> 00:07:36.802 to represent a bridge with our
00:07:36.802 --> 00:07:38.790 program at Doctor Mario Stresa.
00:07:38.790 --> 00:07:40.974 Bosco has done a wonderful job
00:07:40.974 --> 00:07:43.158 building a liver cancer program over
00:07:43.158 --> 00:07:45.798 many years and we still plan to work
00:07:45.868 --> 00:07:48.157 very closely with he and his team.
00:07:48.160 --> 00:07:48.816 In addition,
00:07:48.816 --> 00:07:50.456 we have started and launched
00:07:50.456 --> 00:07:51.980 for disease specific programs,
including pancreas,
neuroendocrine advanced hepatic
bilary and colorectal ING.
 Alone.
I'll speak about those in just
a moment and we have some tumor
boards that match up with these,
which we will also talk about.
So we have implemented some
new meetings on the yellow.
The yellow Star indicates things
that have been implemented newly
in the last year, so we have had an
existing trimmer but actually just
yesterday we launched a split, so this
is now a single hour and a half meeting,
but we have an upper GI pancreas net tumor board and a colorectal tumor board. The Liver Tumor Board is still on Thursdays. We have our existing DART clinical trial review, but we started a Center for GI Cancer Seminar series on Thursday afternoons that consists of Journal club being led by Doctor Christie Gomez. Scientifiche talks clinical talks and industry pipeline talks. In addition, we’ve started a number of working groups and committees. This includes a GI tumor board revamp working group.
This initial phase has concluded, but we will continue to meet quarterly a GI multi D Clinic working group. We started this in March and or having monthly meetings to pilot some multi D clinic switch, I will speak about on a later slide. We have leadership cabinet meetings and program leader meetings. So we’ve been quite busy. So I’ll speak next about our disease programs. I want to mention some shared themes that I won’t repeat on some of the specific slides, but we all envision in the pancreas,
00:09:26.440 --> 00:09:27.88 colorectal advanced hepatic biliary, and net programs to focus on these pillars.

00:09:30.610 --> 00:09:31.994 So multi disciplinary clinics, tumor boards, care coordination really important to GI cancers,

00:09:33.731 --> 00:09:35.119 integration of palliative care and we actually just have newly recruited Doctor Laura Baum who is palliative care and he Monk trained.

00:09:36.540 --> 00:09:38.670 She will join us this summer. In terms of education,

00:09:40.660 --> 00:09:42.750 we plan on expanding physician education and CME events, patient education events,
mentoring with shovel ready, projects for trainees, and plan an advanced fellowship in GI Oncology for research. We hope to expand on clinical trials, specifically Iits. That's something that we need to increase in our portfolio and I will let Doctor Mazumdar speak later about some of our basic and translational research efforts. And then Lastly, I'd like to think of this as the fourth pillar, and particularly in my role as the Vice
Chief for DTI and getting more involved with community engagement and HealthEquity.

I’d like for us to think about these aspects as we do all of our patient care, education, and research.

So the pancreas program is being co-led by doctors Jill Lacy and Mandar Mazumdar.

And in terms of patient care would I have done on these sides?

Is underlying some of the key aspects that are unique to this program that have planned a pilot, so they have planned a pilot, pancreatic cancer multi D clinic with a focus on non metastatic disease.
We have just recently started point of care.

Germline testing with collaboration with Shabbier your and his cancer genetics team.

Advanced endoscopy expertise.

As I’d mentioned, we are embedding palliative care in our program and we had a pink pancreatic cancer early detection clinic in terms of education.

We are hoping to launch a pancreatic cancer interest group for trainees and then in terms of Community wide efforts, we had a very successful Yale Pack seminar series this past year under Research Summit led by Mandor.

In terms of research,
50% of our new pancreas patients are consented into clinical trials and we have been the leading in roller for clinical trials in the US between 2016 and 2019, we treated over 400 patients, 38% at care centers from clinical trials, and we plan to grow the IIT. Samples and this represents 61% of all of our biorepository samples, so that’s a problem for the other diseases which we will speak to as an opportunity. And then we also plan on leveraging innovative multi omics profiling on the right are some of our recent publications.
The colorectal program is co-led by doctors Michael Cicchini Shabbier and ready in terms of patient care, we plan on developing a Nurse Navigator program, fully integrating genomics with patient care and developing an early age of onset colorectal clinic in terms of education, we hope to work with stakeholders such as this Milo screening program on public campaigns. This is especially pertinent as the USPS TF guidelines. Roll out for the lower colorectal cancer screening age. And then, in terms of research
for the colorectal program, we aim to enhance collection of colorectal specimen in a GI BIOREPOSITORY and increased clinical trial enrollment, again with IIT’s, and then expand the early age of onset colorectal cancer thinktank. This is a committee that was started by Shawbury Orangel Mamma. And then Lastly, our community outreach and engagement plans for colorectal with developing targeted strategies and special emphasis on underserved populations. The advanced hepatic Biliary program built will link very closely with Mario,
Tresa, Bosco’s liver program.

This is being Co led by doctors, David Madoff, Stacy Stein and Saj Khan and the Patient Care Education and research plans are listed here.

I would say importantly for patient care, we routine tumor profiling for biliary cancers has proven in recent years to be critical in terms of therapy selection.

In terms of education, we will again work. Mostly within the liver cancer program and some of the research plans are very much in line with the other shared programmatical’s. The neuroendocrine tumor program.
I will be Co leading with Doctor Darko Pukaar from nuclear medicine and from a patient care perspective. We plan on launching a pre PRT clinic. For those of you who don’t know, PRT is peptide receptor radionuclide therapy. The agent is 177 Letitia Ndoda Tate and we plan on doing this to really streamline and provide some consistency for heart patients are getting here. In terms of education, we also plan on having more patient events such as Milo, carers and hopefully in person and collaborating with some.
00:14:47.669 --> 00:14:50.008 of our nonprofit foundations.
NOTE Confidence: 0.88139915
00:14:50.010 --> 00:14:51.450 In terms of research,
NOTE Confidence: 0.88139915
00:14:51.450 --> 00:14:52.890 the BIOREPOSITORY is also
NOTE Confidence: 0.88139915
00:14:52.890 --> 00:14:54.279 enriched for nut cases,
NOTE Confidence: 0.88139915
00:14:54.280 --> 00:14:57.484 and we hope to build on this and then,
NOTE Confidence: 0.88139915
00:14:57.490 --> 00:14:59.270 in terms of clinical trials,
NOTE Confidence: 0.88139915
00:14:59.270 --> 00:15:01.686 we have a real opportunity that should be
NOTE Confidence: 0.88139915
00:15:01.686 --> 00:15:04.608 a key site for impactful clinical trials.
NOTE Confidence: 0.88139915
00:15:04.610 --> 00:15:05.190 In fact,
NOTE Confidence: 0.88139915
00:15:05.190 --> 00:15:07.510 we are one of five Centers for a
NOTE Confidence: 0.88139915
00:15:07.581 --> 00:15:09.105 international clinical trial Meter
NOTE Confidence: 0.88139915
00:15:09.105 --> 00:15:12.233 on which I sit on the steering
NOTE Confidence: 0.88139915
00:15:12.233 --> 00:15:14.519 committee and there are a number
NOTE Confidence: 0.88139915
00:15:14.519 --> 00:15:16.436 of other novel peptide receptor
NOTE Confidence: 0.88139915
00:15:16.436 --> 00:15:18.346 radionuclide agents that we hope
NOTE Confidence: 0.88139915
00:15:18.346 --> 00:15:20.268 to examine in clinical trials.
And we have a number of grants in the works that will hopefully start bringing together both Yale Science and outside science. Moving on to patient care. So this data represents new patient visits from both in the tank and Sir junk. This does not include radiation oncology and in our leadership cabinet meetings we have started reviewing data and key performance indicators with the goal to develop a dashboard of GI cancer specific metrics. So as you can see here, this is trends overtime.
We certainly dipped and have really plateaued since the covid pandemic, but we have bounced back.

Another interesting set of data that we looked at then courtesy of Kevin Best was our Connecticut population and distribution of GI Services across our service area, and I think this is helpful for us as we think about developing and placing services in specific locations. So as an example here in red or a GI medical oncology. Providers in yellow GI radiation oncology. And in green GI surgical oncology, so there certainly clustered
at areas of denser population.

Those are in the dark blue,

but I think there are still certainly some opportunities.

Another data slide that I found also especially interesting as we think about sort of strategic planning,

is the incidence of new GI cancers across the state.

We here look at colon stomach, Asafa, Geo liver,

and pancreas the the higher rates for the state are in red and I have kind of squares around the two disease sites where.

Our rates are higher than the US rates,
and that’s true for both stomach and pancreas, and I think that’s perhaps why we actually accrue so successfully to pancreatic cancer clinical trials and have a very robust clinical and research program in pancreas cancer. Would like to also mention you know, like almost everybody, covid has disrupted our outpatient practice. GI Medical Oncology main campus is still on the 1st floor of the North Haven Care Center. I’d like to use this as an opportunity to really thank my nursing partners Ali and seller Ooley Hazare PSM,
Kathleen Moseman and Vanna Dest. We have worked hard to try to make this space work for our team. There are still some challenges for sure, but we’re appreciative. Of some of the small wins that we’ve had, such as a new counter space and putting in a new workstation. I’ll mention just briefly, our GI tumor burden multi D efforts, so as I had mentioned yesterday, we launched our split of the GI Tumor Board. This was initiated due to the incredible growth in our tumor board.
and this is really with credit due to Stacy
NOTE Confidence: 0.8364233

sign and more in the lead and others,
NOTE Confidence: 0.8364233

and in addition the colorectal team would
NOTE Confidence: 0.8364233

like to launch the National Accreditation
NOTE Confidence: 0.8364233

Program for Rectal Cancer and in.
NOTE Confidence: 0.8364233

Order to do so and become an accredited site.
NOTE Confidence: 0.8364233

We are required to have a separate
tumor board so the upper GI pancreas
NOTE Confidence: 0.8364233

tumor board will be led by
NOTE Confidence: 0.8364233

Stacy Stein in the colorectal ****
NOTE Confidence: 0.8364233

tumor board is being led by an poncho
NOTE Confidence: 0.8364233

and hadn’t put out happy and tell.
NOTE Confidence: 0.8364233

This is our actually tumor board
NOTE Confidence: 0.8364233

from yesterday via zoom.
NOTE Confidence: 0.8364233

I’d like to also re late take this
NOTE Confidence: 0.8364233

as an opportunity to thank Lauren
Mallette who does an incredible job with tumor board and the support from other leaders to make this happen. It was a little bit more complicated than I imagined, but to Kevin Billingsley, hell Terra David. Fisher, Sonya, Bricelyn tide Wilcox. Are multi D clinics or a work in progress and we are building on some lessons learned from the earlier colorectal cancer pilot that was done in North Haven and delayed by Covid. We have plans for 2 pilots of colorectal cancer, Dion Trumbull and a pancreas.
multi D at main campus and we have already started some smaller working groups and are meeting regularly to try to think about some strategic planning that includes some of the elements listed here such as enhancing signature of care. Aligning with our existing disease programs. Selecting an optimal location and then later on we will work on operational topics, workflow being creative with Tele health, etc. Lastly, in the round with patient care,
I’d like to mention that our team members make important contributions to the NCC and panels are institutional, representative issues, and Higgins who sits on the NCC and guidelines steering Committee, and she’s been very helpful, helpful with guidance around this. So Stacy Stein serves on the hepatic biliary piano. John Kunsman on the pancreas, panel, Sajc on on the neuroendocrine tumor panel, Jill Lacey on the Asafa Geo. Jill Lacey on the Asafa Geo. Gastric panel in Kim Jong on the small bowel, colon, rectal,
00:20:48.364 --> 00:20:49.221 ****.
NOTE Confidence: 0.8364233
00:20:49.221 --> 00:20:52.828 Channel so let’s move on and talk
NOTE Confidence: 0.8364233
00:20:52.828 --> 00:20:53.744 about education.
NOTE Confidence: 0.8364233
00:20:53.750 --> 00:20:56.494 I’d like to give two of our fellows
NOTE Confidence: 0.8364233
00:20:56.494 --> 00:20:57.770 a big shout.
NOTE Confidence: 0.8364233
00:20:57.770 --> 00:20:59.475 Our papers just gave presentations
NOTE Confidence: 0.8364233
00:20:59.475 --> 00:21:01.611 last week at our fellow research
NOTE Confidence: 0.8364233
00:21:01.611 --> 00:21:03.461 retreat and Doctor Timmel Patel
NOTE Confidence: 0.8364233
00:21:03.461 --> 00:21:05.383 gave a presentation on clinical
NOTE Confidence: 0.8364233
00:21:05.383 --> 00:21:06.887 outcomes or first line,
NOTE Confidence: 0.8364233
00:21:06.890 --> 00:21:09.445 full fear and ox versus Gen Plusnet,
NOTE Confidence: 0.8364233
00:21:09.450 --> 00:21:11.258 paclitaxel in metastatic pancreas.
NOTE Confidence: 0.8364233
00:21:11.258 --> 00:21:13.970 Cancer Timmel is a senior fellow
NOTE Confidence: 0.8364233
00:21:14.046 --> 00:21:15.990 will be graduating this year and
NOTE Confidence: 0.8364233
00:21:15.990 --> 00:21:18.574 has taken a job with the FDA where
NOTE Confidence: 0.8364233
00:21:18.574 --> 00:21:20.764 he will serve as a medical officer
So in this study, Timol and his mentors Gelasia Michael and Gelasia Michael Cicchini wanted to compare overall survival and time to treatment for two main chemotherapy regimens from metastatic pancreas cancer: Folfirinox and gemcitabine-paclitaxel. They reviewed over 300 patients and found that patients treated with Firstline full paradox had increased survival. These patients were younger and less likely to be admitted while on treatment and rates of treatment discontinuation. Due to toxicity, the two regimens were actually similar.
between the two regiments.

Secondly, Doctor James Zang is currently on RT32 training grants. She has one more year left on that she presented on her project at MGM. Her mentors are Doctor Kurt Shelper, Michael Cicchini and Jill Lacey, and her specific aims and I will not go into all of the details on her project, which are were beautifully presented by her. At the specific aims are to quantify MGMT expression in colorectal cancer cohorts and assess Association of MGMT.
expression with DNA damage repair,

adaptive tumor, immune response,

and overall survival,

Secondly review some of these same characteristics in an investigator initiated clinical trial launched by Doctor Cicchini and Tamil Patel using tamazula, my dental lab rib. So very exciting.

In the realm of patient education, we tested out the Smilow shares platform, which was actually very user friendly and lots of fun during colorectal Cancer Awareness Month. In March we gave two separate presentations,
one to the New Haven community and
the other to the Greenwich Community,
and we took advantage of again local
expertise, particularly in Greenwich.
We collaborated with one of the
colorectal surgeons at Greenwich
Hospital and two of our Care center,
medical oncologists,
So moving on to clinical research.
How does the GI DART clinical trial
portfolio compare internally and again?
These are metrics that we are looking
at in the course of our leadership
cabinet discussions. A thank you.
Great thank you to Christina Weishar CTM.
So the GI DART clinical trial portfolio is 8% of YCS overall clinical trial portfolio, yet it represents actually 11% of all the clinical trial accruals. We have proved quite well. And 14% of analytic cases indicating that we could potentially do better. 5% of the GI cancer analytic case volume accrues to clinical trials, so we are higher than the national benchmark. However, the NCI expectation is as much as 20%, so for sure it opportunity to do better, or GI DART sponsor mix is as follows. The ideal is thought to be a third.
a third, so we certainly would like to increase our IIT. Portfolio. Our accrual trends follow the overall YCC accrual trends with a dip during covid and we are now starting to recover and our accrual over the last 12 months has been heavily reliant on cooperative group studies and industry studies. And note that the numbers on this slide represent trials managed by the GI Dark, but we have a number of patients that go on to other other darts, such as phase one. We are grateful and very reliant on our care center colleagues for
accrual to our clinical trials.

In fact, 38% of our clinical trial accruals came from our care centers between 2016 and 2019.

I’d like to highlight two of our investigator initiated clinical trials that first here is pidd by Doctor Jill Lacey.

It’s a phase two study of PERI operative modified folfirinox and localized pancreas cancer.

It’s a single arm study in which patients receive 6 cycles of modified folfrinnox followed by surgery followed by 6 more cycles of modified folfrinnox.

This is actually one patient
away from completing enrollment,
so we’re very excited about
that and I think that.
There will be some very interesting
correlative’s that come along with this.
Doctor Kim Jong is leading another
investigator initiated trial,
a phase two study to evaluate modified
folfirinox and stereotactic body radiation
and nonmetastatic unrespectable key back.
In this study, patients received up
front fulfi Rannoch 6 to 12 cycles,
followed by SPRT, followed by surgery.
There are a number of really.
It’s a very interesting correlative’s
that are multi disciplinary including
NOTE Confidence: 0.8227002
00:26:37.248 --> 00:26:39.738 US elastography with doctors Farallones
NOTE Confidence: 0.8227002
00:26:39.738 --> 00:26:42.760 leniency T DNA with Doctor Patel,
NOTE Confidence: 0.8227002
00:26:42.760 --> 00:26:44.900 molecular and immune future
NOTE Confidence: 0.8227002
00:26:44.900 --> 00:26:46.505 assessment with doctors.
NOTE Confidence: 0.8227002
00:26:46.510 --> 00:26:48.674 Cikini Joshi Farallon Sklar
NOTE Confidence: 0.8227002
00:26:48.674 --> 00:26:50.838 and development of pancreatic
NOTE Confidence: 0.8227002
00:26:50.838 --> 00:26:52.410 organoids instructor Joshi.
NOTE Confidence: 0.83298975
00:26:57.730 --> 00:27:00.222 I also would like to really give
NOTE Confidence: 0.83298975
00:27:00.222 --> 00:27:02.648 some kudos to Doctor Michael Cicchini
NOTE Confidence: 0.83298975
00:27:02.648 --> 00:27:05.630 who has just received his KO 8,
NOTE Confidence: 0.83298975
00:27:05.630 --> 00:27:08.038 so this is really a beautiful combination
NOTE Confidence: 0.83298975
00:27:08.038 --> 00:27:10.769 of the clinical and translational research.
NOTE Confidence: 0.83298975
00:27:10.770 --> 00:27:13.586 So the title of his Kaylie does DNA
NOTE Confidence: 0.83298975
00:27:13.586 --> 00:27:16.518 damage as a tool to enhance the
NOTE Confidence: 0.83298975
00:27:16.518 --> 00:27:18.668 immunogenicity of cold GI tumors.
NOTE Confidence: 0.83298975
His mentorship committee is listed here.

His aims in his K-8.

I’ll just read them and won’t go into the details.

But it is to perform clinical trials with novel combinations of DNA damaging agents for patients with MGMT promoter hypomethylated colorectal cancer to identify predictive biomarkers for novel alculator combinations in CRC and Tour desk, assess DNA damage is a tool to enhance the immunogenicity of cold colorectal tumors.

I’d like to end with a couple of new projects that we’re working on. This one is actually very exciting and
I'll give a little bit of a teaser and think Roy and add Captain and I are talking about finding another forum, but we are working on a clinical trial matching project in GI oncology with Guangdong and Wade Schultz and a team to really determine if we can match patients to the clinical trial at the right time, accurately efficiently with high volume in a project that's scalable. Other team members included Kathy and Christina Weiss, myself in your fish back. We are using this clinical trial on its Michael Cicchini is tamazula.
My dental lab rib study.

As a pilot we’ve selected for inclusion criteria in which Gwen and Wade and their team use natural language processing and structuring data from the EMR.

This is the workflow focus on the orange box and we are using the entry event in the pre screening event as pilots right now.

Just to give you a sense of the numbers, we that blue top line looks at the number of visits to GI Oncology Department by week followed by the number of patients unique patients to GI oncology by week, then down in Gray.

The number of patients with colorectal cancer than those with metastatic stage four,
and then ultimately that bottom line where you see the numbers in red range from 10 to 15 patients per week that could potentially be eligible for this clinical trial.

How great would it be if you got in your inbox? A list of eligible patients every week for your individual trials.

So this pilot was incredibly effective and efficient. It had about a 98% accuracy rate and it really cut down on the amount of time. So before we estimated 3.11 minutes per chart for 10 week full time.
00:29:46.477 --> 00:29:48.557 working hours and afterwards 1.82
NOTE Confidence: 0.8166703
00:29:48.557 --> 00:29:50.987 minutes per chart which just equals
NOTE Confidence: 0.8166703
00:29:50.987 --> 00:29:53.825 three days of full time working hours.
NOTE Confidence: 0.8166703
00:29:53.825 --> 00:29:57.095 So I’m really excited to see
NOTE Confidence: 0.8166703
00:29:57.095 --> 00:29:59.360 where where this goes.
NOTE Confidence: 0.8166703
00:29:59.360 --> 00:30:02.125 Lastly,
NOTE Confidence: 0.8166703
00:30:02.125 --> 00:30:04.160 Aryel GI tumor biorepository is a
NOTE Confidence: 0.8166703
00:30:04.160 --> 00:30:07.360 real foundation for our program.
NOTE Confidence: 0.8166703
00:30:07.360 --> 00:30:09.360 This is being PII by by Doctor John,
NOTE Confidence: 0.8166703
00:30:09.360 --> 00:30:11.574 Councilman and the technician Joanna,
NOTE Confidence: 0.8166703
00:30:11.574 --> 00:30:14.559 who it’s been in existence since
NOTE Confidence: 0.8166703
00:30:14.560 --> 00:30:17.360 2012 and we have over 1100 patients,
NOTE Confidence: 0.8166703
00:30:17.360 --> 00:30:20.560 but it certainly has, like many things,
NOTE Confidence: 0.8166703
00:30:20.560 --> 00:30:23.185 taken a bit of a hit during covid.
NOTE Confidence: 0.8166703
00:30:23.185 --> 00:30:25.360 John has really taken this as an
NOTE Confidence: 0.8166703
00:30:25.360 --> 00:30:27.695 opportunity to revamp and modernize,
so our accrual numbers have certainly increased overtime or biorepository. Is over represented with colon, rectal and pancreas tumors. We certainly hope to expand on this. And as I’d mentioned, John really has revamped the infrastructure, so we have an existing steering committee, but we now actually have a new location and BML. We have a brand new freezer and John has completely overhauled the consent and intake process to reduce the survey link for patients and to add explicit language for modern.
research activities such as multi-omics cell lines and organoids and deposition of anonymized data in the public repository's. And we have a number of examples of active projects including a study in pydoc with UCLA and then Elappara Bram study on this multi-institution study. So we have a number of future needs, including more, broader and more diverse tumor collection, resumption of specimen collection in our care centers and updating our database. I'm going to just end with a mention of some really exciting work that Wade Schultz and his team are doing to use...
a computational health platform to build an integrated clinical database. So imagine. That you have all of your structured EHR data, imaging, pathology, genetics, all of these data sources. You put it into a funnel and this is a essentially a workflow you can create curated data by the use of red cap and then Wade and his team create aid and integrated user interface so that it really minimizes redundancy of manual data entry. The CHP news cases include COVID-19, in which they were.
The teams were quite prolific.

Hematology is just starting to launch this and integrating a number of key structured databases including C, Bioportal, Redcap omaf genomic data in registry data.

So to end, you know, I think that we have a number of strengths. We have a high patient volume within our network. We have a large clinical trial and financially healthy portfolio.

Still that we're hoping to maintain. We have an existing and expanding biorepository and strong basic and translational science.
I think we have a lot of opportunities in the next one to five years, including expanding our clinical trial portfolio with IIT’s. I think really investing and expanding and the Biorepository, I think that will help us help lead us to better team science and then in the long term or medium term goals of obtaining multiply and program project funding. So I will stop there.

And pass the baton to Amanda, and then we’ll take questions after right?
Thanks, Pam. I think we should move on to Amanda and then we'll do questions at the end. Please put your questions in the chat. I know I have a few for you, but now we're very fortunate to have Mandar was Amdar who is assistant professor of genetics and Medicine. He's part of the Yale Cancer Biology Institute, threes at West Campus, and my Dream is one day will hold one of our grand rounds in person on West Campus. I promised that tomorrow I'm We will hold to that scientific director
00:33:46.359 --> 00:33:48.260 of the Center for Gastrointestinal Cancers here at the hospital

00:33:48.260 --> 00:33:50.320 and just quickly his background.

00:33:50.320 --> 00:33:54.894 He’s also has a Stanford background medical degree from Stanford

00:33:54.894 --> 00:34:00.331 and then internship residency at Brigham and Women’s Hospital, Dana Farber Cancer Institute.

00:34:00.340 --> 00:34:03.444 And then he completed his postdoctoral research at the Koch Institute of Integrative Cancer Research at MIT, so a lot more I can say about manager, but I will.

00:34:03.450 --> 00:34:05.616

00:34:05.616 --> 00:34:07.960 research at the Koch Institute of

00:34:07.960 --> 00:34:10.055 Integrative Cancer Research at MIT, so a lot more I can say about manager, but I will.

00:34:10.060 --> 00:34:13.552

00:34:13.560 --> 00:34:14.520 and I’m Amanda.
The floor is yours.

Great thank you Roy for the kind introduction.

I just want to build on what Doctor Kunz is described and talk a little bit more about up challenges and opportunities in translational research, specifically in GI cancers at Yale.

So I’ll briefly discuss some more detailed metrics on the current state of GI Cancer Research at Yale and then talk about some of our goals in building translational Sciences within the center. Describing four specific overarching initiatives.
Distance shown here and then, talk a few.

A bit about some of the more specific initiatives that we have planned using pancreatic cancer and the Yale Pancreatic Cancer Collaborative is an example of the types of things that we’re hoping for.

So I’d like to start by saying that GI Cancer Research at Yale within the Cancer Center is prolific.
From July 2019 to December 2020, and as you can see, there were more than 130 publications for GI cancer related research within this 18 month time span, amounting to about 7.5 publications per month, which I personally thought was quite impressive given that many of our investigators were dealing with the pandemic during this time. Importantly, more than 1/4 of these publications, four published in high impact journals, and they represented the full spectrum of diseases within.
The GI space, including pancreatic cancers, colorectal and gastroesophageal liver cancers. Furthermore, these publications included 47 individual investigators within the Cancer Center. Again, quite a diverse crew including basic scientists, clinical and translational scientists, and epidemiologists. Now the story is very similar for active research funding where the GI cancer portfolio includes nearly $5 million.
00:36:16.871 --> 00:36:20.789 million in direct costs of research funding.
NOTE Confidence: 0.83620965

00:36:20.790 --> 00:36:23.695 This is about 2/3 in peer reviewed.
NOTE Confidence: 0.83620965

00:36:23.700 --> 00:36:27.276 Either NIH or competitive foundation grants.
NOTE Confidence: 0.83620965

00:36:27.280 --> 00:36:29.548 And the remaining from industry or
NOTE Confidence: 0.83620965

00:36:29.548 --> 00:36:31.540 non peer reviewed foundation grants.
NOTE Confidence: 0.83620965

00:36:31.540 --> 00:36:34.284 You can see there is a heavy influx
NOTE Confidence: 0.83620965

00:36:34.284 --> 00:36:37.319 of money focused on pancreatic cancer,
NOTE Confidence: 0.83620965

00:36:37.320 --> 00:36:40.015 but there is a good spread across
NOTE Confidence: 0.83620965

00:36:40.015 --> 00:36:41.870 the different disease programs.
NOTE Confidence: 0.83620965

00:36:41.870 --> 00:36:44.950 Additionally,
NOTE Confidence: 0.83620965

00:36:42.310 --> 00:36:44.950 this funding has been accumulated by
NOTE Confidence: 0.83620965

00:36:44.950 --> 00:36:46.671 24 independent investigators with
NOTE Confidence: 0.83620965

00:36:46.671 --> 00:36:49.086 a very similar spread in the basic
NOTE Confidence: 0.83620965

00:36:49.086 --> 00:36:50.950 clinical translational epidemiologic space.
NOTE Confidence: 0.83620965

00:36:50.950 --> 00:36:53.428 Importantly, most of these funding sources,
NOTE Confidence: 0.83620965

00:36:53.430 --> 00:36:55.490 in fact, the vast majority,
are really independent grants,

single investigators,

and so the hope is to really love

leverage this great breath.

Of scientific expertise,

clinical care,

and clinical research expertise

and try and build and synergize

their efforts into teams,

and that’s sort of the major goal

of where we’re going to go with

the GI Cancer Center.

So again,

one of our major goals is to build

across display research teams
that bring together clinical, translational, basic and population health scientists. With the plan to allow these teams to enable team based research grants including multi P IR ones, PO1. Since for grants to try and grow investigator initiated trials based on yell science Doctor Kunz, allude to the fact that less than 20% of our current grants are investigator initiated would like to bump that up to at least a third if not a half really showing. Sort of the importance of science within Yale and and what can result
in terms of translational care. And finally, we’d like to use these teams to inspire trainees towards the Korean translational. She, like Cancer Research Doctor Kunz highlighted several of our trainings doing really exciting science within this space. We like to recruit even more exciting science within this space. We like to recruit even more trainees doing really exciting science within this space. We like to recruit even more. Ultimately, the goal is to make Yale’s destination Center for GI cancers such that Yale is synonymous for outstanding.
not only clinical care, but also homegrown science. That translates to the clinic. Now there are number of challenges that get in the way of boosting translational science in GI cancers. Indeed, these are challenges that Roy could speak to for thoracic or even other cancers, and also challenges that exist across the academic spectrum, and these include a lack of time and these lack of institutional resources, a lack of knowledge or expertise, or even awareness of potential collaborators within the institution.
And as team-based science is increasing.

Ensuring adequate recognition or opportunities for career advancement.

So in terms of overarching initiatives to combat these particular challenges, we've come up with four.

One is to really emphasize community building, which is hopefully to bring awareness of potential collaborators, and expertise, and that can be leveraged towards team-based grants.

Additionally,
try to enhance research education
across spectrum to try and get
basic scientists to communicate
with clinical scientists and vice versa to enhance knowledge and
bring together teams.
The third pillar is to develop resources
that’s both financial in terms of grants and funding pilot funding,
but also institutional resources for tissue resources such as bio banks
that are hard to come by and hard to leverage within individual labs.
And finally, we like to take advantage of these
great developments and disseminate
it to the Community using web based or social media platforms as an opportunity not only to tell everyone what a great place Yale is for GI Cancer Research and clinical care. But also potentially to recruit outside funding to support some of these others. So to start to chip away and sort of build some of these pillars, a group of us started the yellow Pancreatic cancer collaborative. Shown here is the steering committee that includes Mary leaders in pancreatic Cancer Research and
clinical care across different divisions and departments. Including medical oncology, radiation oncology, surgical oncology, gastroenterology, pathology and the basic sciences.

We formed the Yale Pack, which is an inclusive team of physicians, scientists and trainings that seeks to synergise the strengths of the science and clinical expertise to accelerate transformative research and pancreatic cancer. We held a summit for Community building last August.
This was an entirely virtual summit that included more than 130 participants. Importantly, more than a third of whom were trainees in participation included 16 different departments and three institutes. We had 16 different speakers who either were actively pursuing pancreatic Cancer Research initiatives or those shown in red had not previously been involved in pancreatic Cancer Research to highlight existing research, as well as to engage. Scientists with innovative technologies that could be applied to this research.
space and through these efforts, we've been able to actually generate some teams. I'll describe a few here of examples of multidisciplinary teams in GI cancers, one of which is involves our own lab in collaboration with the key being endocrinology and genetics and computer science, in which we have been studying and identifying a novel endocrine-exocrine hormonal signaling axis that is a driver. Pancreatic ductal and questionable progression in obesity.

Luisa Escobar hires in radiation therapy,
NOTE Confidence: 0.8392697
00:42:03.270 --> 00:42:05.634 has partnered with Jeff Townsend by
NOTE Confidence: 0.8392697
00:42:05.634 --> 00:42:07.686 Statistics John Chrisman and Surgery
NOTE Confidence: 0.8392697
00:42:07.686 --> 00:42:10.128 and Nick Joe Sheehan immunology to
NOTE Confidence: 0.8392697
00:42:10.128 --> 00:42:12.090 understand RNA splicing and tumors,
NOTE Confidence: 0.8392697
00:42:12.090 --> 00:42:14.868 adaptation and a tumor immunity building
NOTE Confidence: 0.8392697
00:42:14.868 --> 00:42:17.566 off really seminal science from the
NOTE Confidence: 0.8392697
00:42:17.566 --> 00:42:19.888 Escobar Hoyos slab that identified a
NOTE Confidence: 0.8392697
00:42:19.888 --> 00:42:23.301 novel role for Mutant P 53 and splicing
NOTE Confidence: 0.8392697
00:42:23.301 --> 00:42:25.013 regulation and pancreatic cancer.
NOTE Confidence: 0.8392697
00:42:25.020 --> 00:42:27.512 Both of these teams based grants have
NOTE Confidence: 0.8392697
00:42:27.512 --> 00:42:29.862 been recently funded by the Damon
NOTE Confidence: 0.8392697
00:42:29.862 --> 00:42:31.478 Runyon Rachleff Innovation Award,
NOTE Confidence: 0.8392697
00:42:31.480 --> 00:42:34.045 highlighting that these team based
NOTE Confidence: 0.8392697
00:42:34.045 --> 00:42:37.129 approaches are really well received by
NOTE Confidence: 0.8392697
00:42:37.129 --> 00:42:39.769 funding organizations in the NCI alike.
NOTE Confidence: 0.8392697
The Teen Challenge awards that have been pioneered by the Cancer Center have also funded several GI cancer related teams.

I'll highlight two of them here. This one, led by set hers on in chemistry that tries to examine the molecular cancer microbiology and the underpinnings of microbiome associated carcinogenesis. Building on work from South Arizona and collaborator Jason Crawford and synthesizing the Genotoxin. Cali Bactine, which is thought to be an inducer of colorectal cancer.

And leveraging this kind of seminal...
pre clinical work to understand pathogenesis by which microbiomes promote cancer in particular colorectal cancer.

And another grant funded by the Teen Challenge Award is includes Auto Group in collaboration with John Wessel, Mirsky, Anne Rd, Hoffer and Comparative Medicine which seeks to define the effects of dietary fatty acids on breast cancer and pancreatic cancer progression, leveraging innovative high fat diets that represented the diversity of bias.
found in human cancers and trying to identify effects on host Physiology as well as on tumor progression and you can see there's a diversity of effects. On pancreatic cancer progression using these diets. Beyond building teams, we've also been interested in educating these teams on the latest and greatest advances and basic science and clinical and translational science by forming the Yale Pancreatic Cancer Collaborative Seminars series. This included an outstanding cadre of investigators, principally outside of Yale,
who encompass that Breath of basic
two clinical science,
as shown here,
and was an opportunity for our
community to learn about.
and to try and build upon some of
what has already come before us and
really understand the unmet needs in
this space and how Yale could position
itself to meet these particular needs.
Another core initiative for our group is
to really build resource development.
Doctor Kunz highlighted the GI cancer
Biobank, which is actually quite prolific, includes a large number of samples in the pancreatic cancer and co-director cancer, and specifically and beyond. Expanding this to other cancers in the GI space.

We’ve also been working closely with their collaborators in surgery, Yelp, Pathology, and Lab Medicine to develop new living cancer models. Based on these perspective collection of samples. These include patient drives into graphs and patient derived organoids with the hope of developing and
molecularly characterizing some of these very precious tissues. Now importantly, many of these tissues are quite limited, particularly in diseases like pancreatic cancer, where the tumor fraction is quite low, and so we need to be able to leverage emerging technologies that are able to garner a large quantity of information from small and scarce samples. Answer To that end, our collaborative has tried to bring together innovative scientists such as Stephen weighing in genetics as Step...
and wrong thing and biomedical engineering who developed interesting multi omics technologies that allow spatial analysis of gene expression, protein expression and even 3D genome organization in very scarce tissue based samples. And so we're excited of the possibility of taking advantage of the Bio Bank to do deep molecular characterization to build resources that could be leveraged. Or to address particular questions that our investigators might have. And finally, I think it’s important for us to be able to expand and let the community know
00:46:25.635 --> 00:46:27.809 about our translational science efforts.

00:46:27.810 --> 00:46:29.875 Shown here are the breakthroughs

00:46:29.875 --> 00:46:31.940 magazine this year that highlighted

00:46:32.001 --> 00:46:34.113 the team building that we’ve done

00:46:34.113 --> 00:46:35.950 in the pancreatic cancer space.

00:46:35.950 --> 00:46:38.085 And shown here also is the ability

00:46:38.085 --> 00:46:40.244 to use Twitter to really expand our

00:46:40.244 --> 00:46:42.456 reach of our center and in hopes

00:46:42.456 --> 00:46:44.778 of not only educating the community

00:46:44.778 --> 00:46:46.936 but also potentially as a fund

00:46:46.936 --> 00:46:48.596 raising mechanism in the future.

00:46:48.600 --> 00:46:50.763 So what are some of the future

00:46:50.763 --> 00:46:52.834 specific plans we have in mind

00:46:52.834 --> 00:46:54.270 to meet these initiatives?

00:46:54.270 --> 00:46:56.335 One is we like to expand the
activities we’ve done in pancreatic cancer to the other centers to focus on community building through a similar types of summits or seminar series across our core programs. We’d also like to develop some cross program initiatives within the center. Importantly, we want to focus on physician scientist recruitment in GI cancers. I think they serve as. And in the center from Michael Instagram Cology, which is actively pursuing junior physician scientists, recruits and we hope to be able to bring in more who have a real focus in GI cancers.
We also want to try and bridge the gap between basic and clinical scientists, and to do that, we’re going to try and launch the doctors in series. This is a series to allow clinicians to educate basic researchers on the diagnosis, treatment, and importantly, the unmet needs. For specific answers only. This will these be important community building events, but also an opportunity to educate our basic science community on the challenges faced in the clinic. We want to include basic and translational research talks into the CME events within.
our community that Doctor Kunz described as an education initiative, but also an opportunity for outreach. We want to facilitate team based grant funding, in particular trying to take advantage of internal support such as TCA. The team challenge awarded the teacher grants and ultimately to direct these teams and support these teams administratively towards developing or program project grants. Just peel ones and spores we want to increase Accessibility in Electro characterization of biobank samples.
NOTE Confidence: 0.7921766
00:48:37.890 --> 00:48:39.936 some initiatives in the computational side.
NOTE Confidence: 0.7921766
00:48:39.940 --> 00:48:41.692 We also want to leverage some
NOTE Confidence: 0.7921766
00:48:41.692 --> 00:48:43.720 of the multi omics technologies.
NOTE Confidence: 0.7921766
00:48:43.720 --> 00:48:45.580 And finally we want to fundraise
NOTE Confidence: 0.7921766
00:48:45.580 --> 00:48:47.303 towards the center and disease
NOTE Confidence: 0.7921766
00:48:47.303 --> 00:48:49.418 programs to support this translation.
NOTE Confidence: 0.7921766
00:48:49.420 --> 00:48:51.612 Research clearly to be able to build these
NOTE Confidence: 0.7921766
00:48:51.612 --> 00:48:53.797 teams and provide private pilot funding.
NOTE Confidence: 0.7921766
00:48:53.800 --> 00:48:55.464 Some amount of philanthropy
NOTE Confidence: 0.7921766
00:48:55.464 --> 00:48:57.544 is going to be required.
NOTE Confidence: 0.7921766
00:48:57.550 --> 00:48:59.518 And to do that we want to create
NOTE Confidence: 0.7921766
00:48:59.518 --> 00:49:01.161 a unified Twitter and website
NOTE Confidence: 0.7921766
00:49:01.161 --> 00:49:03.345 presence to really unify the center,
NOTE Confidence: 0.7921766
00:49:03.350 --> 00:49:05.660 but also to make key announcements
NOTE Confidence: 0.7921766
00:49:05.660 --> 00:49:07.200 of advances in translational
NOTE Confidence: 0.7921766

86
science within our center.

And so with that, we're happy to take any questions.

Thank you both. That was absolutely wonderful. Well, we'll put some some questions in the chat,

Pam can you speak a little bit about you talked about screening for colorectal cancer? Can you talk about what the current guidelines are and how we're addressing that here? At? Yes, my own.

Also, the whole HealthEquity issue around this.
How are you making sure that all patients are getting in for a screening? So, so at present the recommended screening age is still 50 on the USPS TF guidelines. The draft has not been accepted into practice just yet. So what I will say, I have an in since my husband is a gastroenterologist in the community, but he has said that I think this is appropriate that we recommend if patients who are between the ages of 45 and 40 interested that they check with.
their insurance company first.

I mean, I anticipate that this will in fact be adopted and then we will.

Have a considerable education to do and I think that partnering with the colorectal cancer program Shabbir died and his team.

We talked a lot about outreach and how we can improve our efforts in that space.

Right, you mentioned you’re using Wades database.

Are you able to look through that database by the patients that you’re screening, representing the Community in general,
00:50:38.040 --> 00:50:39.470 or their areas to enhance?

00:50:41.000 --> 00:50:43.696 So we are just starting working with Wade,

00:50:43.700 --> 00:50:45.891 but that’s an excellent idea and I

00:50:45.891 --> 00:50:48.316 think ways that we can leverage that

00:50:48.316 --> 00:50:50.452 and also with Marcelonis Smith.

00:50:52.310 --> 00:50:53.970 Amanda, why is pancreatic cancer

00:50:53.970 --> 00:50:55.630 so difficult to to treat?

00:50:55.630 --> 00:50:57.954 You know, you have these new new

00:50:57.954 --> 00:50:59.328 approaches, but immunotherapy.

00:50:59.328 --> 00:51:02.160 It doesn’t seem to work as well there

00:51:02.232 --> 00:51:04.255 as in many of the other cancers.

00:51:04.260 --> 00:51:05.920 What’s the reason for that?

00:51:07.150 --> 00:51:09.734 Yeah, I think there’s a number of kind

00:51:09.734 --> 00:51:12.480 unique features of pancreatic cancer,

00:51:12.480 --> 00:51:14.420 in particular that make it
particularly challenging for therapeutics and even therapy space. It's well known that pancreatic cancer has a quite a bit of a different stromal microenvironment. In particular, it's thought that this microenvironment made up of fibroblast immune cells, like macrophages in particular, as well as exercising matrix proteins, can be quite immunosuppressive, and even in mismatch repair deficient. Pancreatic cancer is the response. Rates are quite a bit lower than, for example, what we’d see in colorectal cancer,
suggesting that there's something unique about the intrinsic biology of pancreatic cancer, and I think the stroma quite plays quite a bit of a role. Importantly, pancreatic cancer is genetically fairly bland. It gets 4 hallmark recurrent genetic alterations, in particular in the proto oncogene carass, and three other tumor suppressor genes. So in terms of targetable genetic alterations, there are few. And even within care as mutations
there currently targetable 1G12C mutations are quite rare, only found by two to 3% in our own data suggested that even if you had a perfect chaos inhibitor, resistance is likely to emerge at least half of the cases, and so I think there are a number of factors that lead to the poor outcomes of pancreatic cancer, and I think one aspect that deserves more attention is prevention in the disease. One of the key factors to poor outcomes is often late stage of diagnosis, where more than 80% of patients
are found at a time when they’re not surgically resectable, which really is the mainstay curative option in this disease, and So what can we do to understand when this disease emerges? Can we intervene earlier? Can we identify earlier disease, and can we even develop strategies for prevention by understanding risk factors? For example, how they play a role, and that’s sort of driven some of our own efforts in the obesity. Pancreatic cancer space. Other genetic risks as well and I
have to use big data AI approaches.

Do you think we'd find some genomic factors that might tell us who might need need to be screened earlier?

Yeah, there are a number of genetic factors that have been identified only about 10% of pancreatic cancers are thought to be familial in nature, and a subset of those patients will have known genetic alterations and our screening clinic here. Led by James Farrell, is focused on that in trying to. Follow these familial cases not only in terms of genetics, but also to understand other risk.
factors such as new onset diabetes.

And it turns out about 1% of pancreatic cancer cases can be identified when you want to diabetes.

Could we use that as a biomarker of sort of early detection?

And so there are a number of avenues that people are exploring, and certainly big data type approaches that mirror that match.

Clinical prior clinical history again may be taking advantage of.

EMR mining, like Wade Schultz is doing, could help identify some of those
patients and identify other risk factors and their number of groups, including the Dana Farber Group that is trying to build risk scores. That combined with genetics as well as non genetic factors to truly determine who are perhaps the most highest risk.

And finally, we still need to further optimize. What are the best screening protocols? Is it a combination of endoscopic ultrasound imaging, blood based biomarkers? All of those are active areas investigation.
so Pam, you’re very modest.

I actually, I’m waiting to see how you do the GI program and I’m at all the long program after you you just fantastic and I have to just compliment you coming here during this very difficult year and telling this amazing group together between the campuses and I just think it’s remarkable and I guess zoom has helped a little bit but hopefully at some point we’ll see each other in person.

But how do you clinically with care on going at 15 different care centers?
picture where you actually. All the different people, how are you putting practice plans in place and knowing that someone who goes to North Haven versus someone that goes to Greenwich or Main campus is getting the same sort of approach and care for one of these diseases? That's a great question. You know, I'd say that the first step has been creating forums where our team members will get together and I have to say that we've had just really tremendous virtual attendance, and I think that's one silver lining of the zoom format is that we have no
30 to 40 people attending tumor board, averaging 40 patients attending our seminar series, and those that’s really community building. I think Mandar spoke to that as well, and I think as soon as we have that as a foundation, it creates other opportunities for collaboration. I’m Julie, she is our Director of Education in our leadership cabinet and I know that. She’s told me this, but I think I can say this, but I think she’s she and I and the team are really eager to work on
00:56:15.373 --> 00:56:17.550 that signature of Karen and talking.
NOTE Confidence: 0.8391838
00:56:17.550 --> 00:56:19.416 That’s why we have Journal clubs.
NOTE Confidence: 0.8391838
00:56:19.420 --> 00:56:21.250 We talk about standard practices very
NOTE Confidence: 0.8391838
00:56:21.250 --> 00:56:23.459 openly with all of our team members,
NOTE Confidence: 0.8391838
00:56:23.460 --> 00:56:26.330 and we have really tremendous.
NOTE Confidence: 0.8391838
00:56:26.330 --> 00:56:27.820 Dissipation from our care center
NOTE Confidence: 0.8391838
00:56:27.820 --> 00:56:29.012 members and you know,
NOTE Confidence: 0.8391838
00:56:29.020 --> 00:56:31.106 I think that’s helped by Jeremy Corbyn’s.
NOTE Confidence: 0.8391838
00:56:31.110 --> 00:56:32.610 Key really being an integral
NOTE Confidence: 0.8391838
00:56:32.610 --> 00:56:33.810 part of our team.
NOTE Confidence: 0.8391838
00:56:33.810 --> 00:56:36.250 He has been for a long time and I think
NOTE Confidence: 0.8391838
00:56:36.319 --> 00:56:38.888 infusing his role that’s helping as well.
NOTE Confidence: 0.79950714
00:56:40.580 --> 00:56:40.853 Absolutely,
NOTE Confidence: 0.79950714
00:56:40.853 --> 00:56:43.310 I would just at the end of the hour.
NOTE Confidence: 0.79950714
00:56:43.310 --> 00:56:44.680 Any other questions or comments?
NOTE Confidence: 0.79950714
00:56:44.680 --> 00:56:46.584 One thing I’ll ask you mentioned it.
You make sure Lacey ask both of you.

I see a lot of fellows on the line.

One of the groups is fellows room, so I guess there hopefully had getting a solution there.

If not, let me know for next week, but the question is, do you have projects you know our fellows and we have great fellows? Medical students might even be some undergraduates listening.

I don’t any one of their projects.

How it’s one find a project in GI cancer Mandar.

If they wanted to work in the lab.
or between a lab in the clinic,

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or Pam in the clinic,

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can you let us know?

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Yeah, I think one of our goals

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is to make very accessible shovel

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ready projects for people with

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limited time medical students,

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residents, fellows and I think

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there are a couple of advantages.

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The one is the biobank

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which is quite expensive,

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particularly in again pancreatic

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cancer and colorectal cancer that

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might allow tissue based analysis

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that might be more efficient.

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The second is we have a
large number of patients, particularly the pancreatic cancer space, that we followed for many years, and so some of this studies, for example, what? Doctor Patel has done is based on those types of retrospective analysis and this clinical database that we have in GI cancers. And so again those types of projects are probably much more numerous and we need to make those clearer and make them more shovel ready so that we can get our trainees involved quickly.
In any further I'll just yeah,

I'll if I can just add right,

you know we had our one of our programs director’s meetings last week and we as a those four programs,

all the code leaders identified as our next top priority doing just that of really developing this list

as we have new trainees coming in July and having that available.

Right, and you guys are great.

Actually one big part of the shovel is the handle,

which is the mentor ship and on these projects you don’t want to have a good idea,

but you know it’s I can tell you
from my own career it's having mentors and people that help you so I can see you have that. And plenty of that in the GI Group will look forward to having you back in six months or so to hear more progress, maybe bring some other members of the group, but this is been a fantastic grand rounds today. Will look forward to your first grand rounds for the GI program with an invited guest from Puerto Rico in two weeks and. Thank you all. Thanks everyone for coming today and we'll see you back next week.
00:59:03.671 --> 00:59:05.096 for Cancer Center grand rounds.
NOTE Confidence: 0.8201183
00:59:05.100 --> 00:59:05.690 Thank you.
NOTE Confidence: 0.8201183
00:59:05.690 --> 00:59:06.280 Pam, Amanda.
NOTE Confidence: 0.9220947
00:59:07.490 --> 00:59:09.482 Thank you, thanks.