0:00:00 –> 0:00:02.148 Funding for Yale Cancer Answers is
0:00:02.148 –> 0:00:04.18 provided by Smilow Cancer Hospital.
0:00:06.41 –> 0:00:08.54 Welcome to Yale Cancer Answers with
0:00:08.54 –> 0:00:10.81 your host doctor Anees Chagpar.
0:00:10.81 –> 0:00:12.585 Yale Cancer Answers features the
0:00:12.585 –> 0:00:14.769 latest information on cancer care by
0:00:14.769 –> 0:00:16.169 welcoming oncologists and specialists
0:00:16.169 –> 0:00:18.513 who are on the forefront of the
0:00:18.513 –> 0:00:20.127 battle to fight cancer. This week,
0:00:20.13 –> 0:00:22.104 it’s a conversation about the care
0:00:22.104 –> 0:00:24.369 of patients with both HIV and cancer
0:00:24.37 –> 0:00:26.785 with Doctor Brinda Emu. Doctor Emu is
0:00:26.785 –> 0:00:28.56 an associate professor of internal
0:00:28.56 –> 0:00:30.926 medicine at the Yale School of Medicine,
0:00:30.93 –> 0:00:34.074 where Doctor Chagpar is a professor
0:00:34.074 –> 0:00:36.02 of surgical oncology.
0:00:36.03 –> 0:00:37.591 Brinda, maybe we can start off by you
0:00:37.591 –> 0:00:39.359 telling us a little bit more about
0:00:39.359 –> 0:00:41.14 yourself and what it is you do.
0:00:41.61 –> 0:00:44.998 Sure, so I am an infectious diseases
0:00:44.998 –> 0:00:47.57 physician and a researcher.
0:00:47.57 –> 0:00:50.468 I’ve been an HIV provider for over
0:00:50.468 –> 0:00:53.531 20 years and my research is also
0:00:53.531 –> 0:00:56.715 focused in this area and it’s
0:00:56.715 –> 0:00:59.727 largely to trying to understand the
0:00:59.727 –> 0:01:02.464 long term impact of HIV infection on
0:01:02.464 –> 0:01:04.77 the immune system and what it means
0:01:04.77 –> 0:01:06.8 for individuals and their health.
0:01:06.8 –> 0:01:09.068 Even after viral replication
0:01:09.068 –> 0:01:10.769 has been controlled,
0:01:10.77 –> 0:01:12.87 so I would consider myself
a viral immunologist. I’ve been working in the field of HIV immunology for about 20 years and have a lab in the division of infectious diseases here, trying to understand the question of how long term viral infection impacts non viral associated conditions, including cancer.

Yeah, so you know Brenda, it really does bring to mind the intersection of HIV and cancer now that HIV is really become more of a chronic disease right that now that we have reasonably good antiretroviral therapy. People are living with HIV for a good long time and we do know that HIV is a disease that does affect. The immune system and we’ve talked on this show quite a bit about how the immune system interplays with cancer. So can you kind of give us a lay of the land in terms of that intersection? Are there certain cancers that are more prevalent in people with HIV? And conversely, does HIV impact how people get and respond to other kinds of cancers that may not be classically HIV associated? Yeah. So those are a lot of
really good questions and and really important as you say, as the field of cancer care is sort of evolving to include therapies that target the immune system. So just to take a step back, you know HIV is a virus that directly infects CD4 T cells, and we’ve been, you know, hearing a lot about the importance of T cells in fighting infections. You know, as it’s relevant for many infections. Including COVID-19, but HIV is unique in that in this virus actually infects those cells and kills them when it infects them so. T cells, as you know, are a critical defense against infections and therefore when HIV infects, people become immunosuppressed and they become vulnerable to other infections as well as some cancers that rely on the immune system in order to propagate. Propagate so in fact that’s how HIV and AIDS was initially recognized in the early 1980s. Is that young. Previously healthy people were coming in for medical care with rare and unusual infections, rare and unusual cancers.
And so, as you alluded to, there were certain cancers that were specifically associated with HIV infection, Kaposi sarcoma, non-Hodgkin’s lymphoma, and cervical cancer. And we saw those cancers at increasing rates back in the 80s and 90s. And for some time afterwards. And it was recognized that it was because patients with HIV and advanced HIV were unable to mount the immune response against those cancers. The as you stated correctly, over the next 25 years, we have really good therapy to treat viral replication and if for the most part when patients are taking up a cocktail of antiretroviral therapies, we’re able to get the HIV viral replication under control, with usually an increase in that CD4 T cell count. But what we’re starting to see is that even though those initial 3 cancers which redeemed AIDS defining cancers are decreasing in incidence, we’re seeing increased numbers of other cancers, and particularly those cancers that we are recognizing as relying on the
immune system to be able to fight them. So so so that the the cancer cancers that patients are presenting with among the HIV population have changed over over the last decade. Because we’re seeing less severe immunosuppression, but patients with HIV do have residual immune dysfunction that may predispose them to some of these cancers. 

So tell us a little bit more about that. What kinds of cancers? Are we now seeing with increased frequency in the HIV population? Yeah, so I. So what? We’re starting to see is, well, there’s a couple of of cancers that that are increased in risk in patients with HIV compared to the general population. And those include still include a those aids defining cancers that I mentioned before. Non hodgkins, lymphoma, KS and cervical cancer. But in addition to that, we’re seeing increased rates of lung cancer, Hodgkin’s lymphoma, anal cancer. Liver cancer had a neck cancer, so these cancers are patients with HIV infection are at increased risk for these particular cancers compared to the general population there.
There are other cancers as well that fall into that category, but interestingly not all cancers are increased in significant rates in patients with HIV, for example, we don’t see an increased rate of most breast cancers or colon cancer or prostate cancer in patients with HIV compared to the general population, and so do we know why there are increased risk with certain cancers as opposed to others. I mean, just thinking about some of the mechanisms by which HIV is transmitted and some of the cancers that you mentioned. It seems to me that there may be a correlation between HIV and HPV. The human papilloma virus is that one of the reasons why we see the increased frequency in some of the cancers that you mentioned. I think that’s correct, and in fact some individuals have actually broken down the cancers that patients with HIV are at increased risk for into those that are virally associated and non virally associated. So HPV is human.
Papilloma virus is a causative agent for cervical cancer. For anal cancer, some skin cancers, and some head and neck cancers. Similarly, other viruses like hepatitis B&C can cause liver cancer, and the infection EV can cause lymphomas. So I think that coinfection with these other viruses. That we know cause cancer do seem to be increased among patients that also have HIV infection. But as an immunologist, it is interesting to me that there are also some cancers that are not associated with HPV. The immune system responds to cancer to viruses that cause cancer. It certainly puts patients at increased risk, but I think the immune systems deserves closer scrutiny because not all of the cancers that are at
increased risk are due to viruses. Certainly we know that the immune system plays a role in fighting some of these cancers, and certainly some cancers have developed a kind of what I like to call the invisibility cloak, where we’re very much like a Harry Potter. They can kind of evade the immune system. That can’t really fight, fight the cancers off. And that’s where immunotherapy kind of comes in. Kind of taking away that. So when we think about that, you know there are particular cancers that have expression of PD 1 PDL 1. Do we know whether those cancers are more likely to occur in HIV infected patients? And is there a difference in terms of how these patients respond to immunotherapy? Yeah, that’s a great question and actually is the hypothesis that our lab was sort of operating under? Because if you think back to the list of cancers that I stated were increased
at risk among patients with HIV, including lung cancer and liver cancer, head and neck cancer, many of those cancers are the same cancers in which that immunotherapy is effective in suggesting. That in fact, it is because patients with HIV infection have an impaired immune response that these are the same cancers that respond to immunotherapy and also the same cancers that patients with HIV see it increase risk because they have impaired immune function. So that raises a really the excellent and critical question is, will immunotherapy work as well in patients with HIV as those without? And you mentioned the PD1 PDL1 pathway and drugs that target that pathway as well as the CTA for pathway are commonly known as immune checkpoint inhibitors and they’re designed to reinvigorate exhausted T cells in order to fight cancer. Having worked in infectious disease, these same pathways that PD one PD pathway for example are also extremely relevant. In chronic viral infection and the PD1 PDL, pathways upregulated in the setting
HIV as it is in other chronic viral infections and so so whether treatment with inhibitors to this pathway will work better or worse in patients with HIV is a bit of an unanswered question. But a really, really important one, and I say it’s unanswered. Because patients with HIV have not been regularly studied in the clinical trials that looked at immune checkpoint inhibitors because of initial concerns about potential toxicity, and therefore we don’t have clinical trial data that tell us for sure that patients with HIV do as well as the general population. So these studies are now being conducted retrospectively to see whether patients with HIV are in fact getting responses at the same level, but this is something that is really understudied and really important, particularly for our patients that have immune dysfunction. To know the answer to so important. Well, we’re going to take a short break for a medical minute, but please stay tuned to learn more about HIV and cancer with
my guest doctor Brenda Emu. Funding for Yale Cancer answers comes from Smilow Cancer Hospital, where the bladder cancer team is at the forefront of bladder cancer treatment and research. Learn more at Yale Cancer Center dot org. The American Cancer Society estimates that nearly 150,000 people in the US will be diagnosed with colorectal cancer this year alone. When detected, early colorectal cancer is easily treated and highly curable, and men and women over the age of 45 should have regular colonoscopies to screen for the disease. Patients with colorectal cancer have more hope than ever before, thanks to increased access to advanced therapies and specialized care. Clinical trials are currently underway. Federally designated comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital to test innovative new treatments for colorectal cancer. Tumor gene analysis has helped improve management of colorectal cancer by identifying the patients most likely to benefit from chemotherapy and newer targeted agents,
resulting in more patient specific treatment. More information is available at yalecancercenter.org. You’re listening to Connecticut Public Radio. Welcome back to Yale Cancer Answers. This is Doctor Anees Chagpar and I’m joined tonight by my guest doctor Brinda Emu. We’re learning about the care of patients with HIV and cancer and the intersection between HIV and immunotherapy in the treatment of cancer. One of the reasons why patients with HIV were not included in those initial clinical trials was for fear of toxicity now that patients with HIV are starting to be enrolled in clinical trials. Was for fear of toxicity now that patients with HIV are starting to be enrolled in clinical trials. Can you talk a little bit about whether they do experience more toxicity and whether that initial fear was justified?
So so I feel like the initial fear you know came out of the the biology that the PD one pathway that we had mentioned is so critical at the level of the tumor for the general population. But in the setting of a global viral infection that pathways upregulated on cells throughout the body. So so I think the concern was. When you sort of unleash those cells that patients with chronic viral infections like HIV and hepatitis C might have worse immune related side effects compared to the general population. Now that we have more experience with using these medications, we know that that is not the case. We there’s been two clinical trials specifically focused on patients with HIV in advanced malignancies. That have studied immune checkpoint inhibitors, checkmate 944 and checkmate 020. That were not powered to test efficacy, they were able to report that there does not appear to be any increased toxicity from immune checkpoint inhibitors in patients with HIV compared to those without, so that is very reassuring and allows us to move forward both with
treatment but also importantly and hopefully more studies to really understand the efficacy of these drugs. In our patients, for patients who have HIV who may get very much to your point, immune related toxicity to immunotherapy. Are there special considerations that need to be taken in terms of how you manipulate the therapy in these patients? Because, as you say, that pathways so critical to every cell, so you know 11 might think that it’s a little bit difficult to kind of say. OK, well, we’ll just stop the immunotherapy. Or we’ll kind of reduce the dose. Are there other other considerations in that population when treating them with immunotherapy that patients and their doctors need to be aware of? The most important thing, I think, is that there are HIV be well controlled. I think that the pathway the the immune checkpoint pathways are really sort of very highly upregulated. In the setting of ongoing viral replication, so I think that it would be very important for every patient with with
HIV to be on effective antiretroviral therapy at the time of receiving immune checkpoint inhibitor therapy. But as I mentioned before and I think this is important for patients and providers, and all of the retrospective studies and the clinical trials that have looked at safety. That initial fear that patients with HIV were going to have worse immunologic outcomes, in fact, is it does not appear to be the case. So I think that is very reassuring. Every study that has looked at immune related adverse events are not increased in incidence. Yeah, but to your point in terms of making sure that your HIV is well controlled, one would think you know we talk on this show a lot about this multidisciplinary cancer management and you know many medical oncologists may not be as comfortable in managing HIV because they are so focused on managing cancer in in patients who. Have HIV, can you talk a little bit about how critical it is to make sure that your HIV doctor is part of that multidisciplinary team and the crosstalk that that individual would have with oncology in terms of the
management of the overall patient? Yeah, and so I think this is so so important and I think that you know medical care and subspecialty care is that it’s very specialized and our patients it’s very specialized and our patients with HIV have unique comorbidities. They have, you know, generally multiple medications that have drug drug interactions. And as we’ve been talking about quite a bit have very unique. Considerations for their immunologic health, so I think the key here is that the oncology treatment team and the infectious disease provider really be coordinated and have an integrated approach for the care of these patients. And certainly you know having HIV adds a whole other level of complexity to quote routine cancer management. You know one of the things. When you think about patients who are on. Antiretroviral therapy and you know, already we’re controlling their immune system. Regardless, is is the issue between how patients with HIV, whether or not they are on immunotherapy or not? How they do in terms of their cancer management and prognosis.
relative to the general population, because in the general population. There may be less concern about how your immune system is going to react to not only the cancer but to therapies, whereas in HIV patients that may be a little bit different.

Can you talk about prognosis in these individuals?

Sure, so unfortunately this is an area where we do see disparities in outcome among patients that have HIV and a cancer diagnosis, and this appears to hold true for many different cancer types. Whether or not they’re increased in incidence or not. So I stated before that you know, most colon cancers and most breast cancers are not increased in incidence and.

Patients with HIV compared to the general population, however, the prognosis, even with with those you know with those cancers are worse in patients with HIV compared to the general population. And there’s a.

You know this is there’s probably. There’s probably reflects many different factors. Certainly there’s a concern that patients
may have inadequate screening and may be present at a more advanced stage, and that may partly be responsible for these poor outcomes. However, large studies that have controlled for stage as well as insurance status and access to care have similar have reported similarly poor outcomes in patients with HIV. Compared to those without and that really sort of emphasizes that there are unique features of the infection that we need to better understand, and this includes studying cancer, biology, and particularly, immune related effects of treatments of the treatment on patients with HIV as well as ensuring that patients get screened and and really importantly, that they receive appropriate cancer treatment and follow-up surveillance. And up until the last couple years there have not been specific guidance or guidelines for patients with HIV receiving cancer treatment, and that has changed. There are now NCCN guidelines that are specifically address patients with HIV, so I hope that some of these
disparities can be improved as we get more attention and more research focused on.

On our patients. Yeah, and one of the questions I have is, you know you had mentioned earlier that it’s so important that patients with HIV who are undergoing cancer treatment should really make sure that their HIV is well controlled. Has anybody looked at the control of HIV? So for example, looking at CD4 accounts and seeing whether that makes a difference both in terms of the risk of developing a cancer as well as prognosis of cancers, whether they’re HIV related or not? Yeah, so yes. And so people have looked at biomarkers of cancer incidents in patients on and off antiretroviral therapy, so I’ll step back and say for sure. You know, being controlled and having significantly decreases overall cancer incidence and so that’s the first thing. But even with control, Of HIV infection, there do appear to be some. Immunologic factors that are
associated with increased cancer incidence, and interestingly, it’s not the CD4 count itself that increases your incidence of malignancy among patients with HIV, but the ratio of CD4 cells to CD8 cells. So there does seem to be immunologic factors that predispose to risk in terms of immunologic factors that predispose or conserve as biomarkers. The prognosis this is an active area of study. This is something that we’re actually looking at in my lab and others as well to see whether there are differences that can be identified within the tumor microenvironment. That may portend a better or worse prognosis with immunotherapy or chemotherapy, because I think we haven’t really studied that in depth before. We don’t know the answer to that, but as we’ve been alluding to. And as we have some data to suggest the microenvironment of the tumor is different, and what that means for prognosis is something that really needs a lot more study, and it because it’s so important. It’s so important.
just mentioned I just found so intriguing was that you found that the phenotype of these CD four cells and CD 8. Cells these immune cells actually is different and can predict malignancy a year prior to diagnosis. Did I hear that right? So that’s incredibly interesting my two follow up questions to that are the following number one. Is it to any particular type of malignancy so that you would know what to expect and #2? What do you do with that information? It’s kind of like you’ve been given a ticking time bomb of you will get cancer in a year. Has it been found that this could be useful in terms of increasing screening or perhaps even prophylactic treatments? Yeah, yeah, I, I think that. You know, I? I think it’s not at a stage that it’s predictive yet, but the meaning that it’s clearly a biomarker that can be clinically useful. But what it suggests is that there are ongoing systemic changes in the immune response in a subset of individuals that may predispose them to cancers. And that’s exactly right.
identify patients at increased risk that you may alter screening early diagnosis. In order to get patients you know diagnosed at earlier stages going forward, this is early data and it’s but it it is different from the general population that we’re seeing changes in the peripheral blood that signify sort of immunologic risk potentially to malignancies that could be used as biomarkers.

Doctor Brinda Emu is an associate professor of internal medicine at the Yale School of Medicine. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at yalecancercenter.org.

We hope you’ll join us next week to learn more about the fight against cancer here on Connecticut Public radio. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital.