**Richard Cormack:** I'm delighted to welcome Dr. Naureen Starling with us today. Dr. Starling, thank you for joining us today. Let's begin, if we may, with your career. How did you first get into the field of oncology?

**Dr. Naureen Starling:** Thank you, Richard. Say, I mean, I think the answer is a mixture of experience, people, serendipity, and mentorship. So I did my journal of medical training at Northwick Hospital in London, which I think kind of makes or breaks you as a doctor. An incredibly busy experience. You see everything.

And I really enjoyed gastroenterology. I don't know what it is about the gut, I just was really drawn to it. And I met an oncologist who was consulting with our patients. And she was really inspirational. And she asked me if I thought about oncology as a career. And I had to admit I hadn't. And so she suggested that perhaps, you know, I wanted to get more experience.

So I went off to Mt. Vernon Cancer Center, and oncology really chimed with me. I liked the interface with research and practice. I liked the relationship I developed with patients. I liked oncologists. And so then with some strong mentorship, you know, at that age you're not sure about the future. You know, all these incredible thoughts, opinion leaders, a bit intimidating. Could I really cut it in the field?

And I got excellent mentorship to say this is a wonderful area. It's only going to develop. You should go for it. And so that really started me on my oncology career. I had to sell it, guys. Did my formal training at the Marsden in 2003 and haven't looked back. I haven't left the Marsden.

**Richard Cormack:** You specialize in bowel, pancreatic, esophageal, and gastric cancers. Can you tell us a little bit about why you focus on these? You said you are fascinated by the gut. But some of the particular challenges in these cancers.

**Dr. Naureen Starling:** So, I mean, I think as many of the audience will know, pancreatic cancer is one of the most challenging cancers to treat. Perhaps, well, possibly some of the worst outcomes of all cancers. Gastric cancer is not far behind. Bowel cancer actually is better in terms of picking up more patients at a curable state. But still, in advance, bowel cancer there's a lot to do.

So for me, the challenge also represented a motivating factor. I think we can do better. I think it's dreadful that we haven't made more progress. So I think that's motivating from a research perspective. I think it's a huge unmet need for patients. We have to do better.

And I think therefore the opportunity is there to make a difference. And I think currently we are in an unprecedented time of scientific data science, technology, development, and discovery. And I think those areas can rightly coverage on these more difficult-to-treat cancers. So that's why I am fixed on these cancers.

**Richard Cormack:** If we focus on this year because obviously this year has been a year like no other in terms of the disruption we've seen, and I know it's had a huge impact on the treatment of non-COVID illnesses and kind of on elective surgeries. Can you talk a little bit about the impact of COVID-19 on cancer care in the UK and how you and your team have adapted in this environment?

**Dr. Naureen Starling:** Yeah, I think for all of us it's been an incredibly challenging time. So at the beginning of the pandemic, honestly, we had never experienced anything like it. There was an extreme anxiety about vulnerability of cancer patients, having surgical procedures, radiotherapy, basically chemotherapy, and other drug treatments and whether we could safely treat these patients. And then there was the a fear of the NHS being overwhelmed in terms of capacity, and cancer and other disease areas, cardiovascular, for instance, not being able to access services.

So incredibly challenging. However, there was an exceptional rate of response and scale of response to that across the country. And just to give my perspective, from the Marsden assistance leader in cancer, from day one people sprung into action. So in terms of treating cancer patients, surgery obviously major curative therapy, a big focus on what we would do then and how we could do that safely. And direction of travel but looking at the experience from China, from Italy, that we needed to establish COVID-free environments and utilize independent sector capacity if necessary.

And so the Marsden and other centers in London, UCLH, Guy’s and Thomas' established COVID-free cancer hubs and rapidly reestablished surgery for cancer patients. That was enormously

helpful.

In terms of other cancer treatments, radiotherapy, now, this is the direction of travel anyway in research, but it just got accelerated and that's good. So giving radiotherapy in more innovative ways. Higher doses, fewer visits to the hospital. We were always heading in that direction, but that got implemented across the UK. And that's being now audited and monitored.

And then in my area, drug therapy, you know, how could we give treatments which were more COVID friendly? The UK government, to its credit, established 160 million pound fund to accelerate access to innovative treatments that perhaps didn't have as much risk or as many visits. And that has been hugely welcomed. I think also we stepped up, you know, other ways of working in the hospital, remote consultations. Again, things that we needed to establish in the NHS just got accelerated a lot.

And then from my own hospital's perspective, the Marsden charities sprung into action and launched a COVID-19 appeal which, you know, Goldman Sachs also generously supported. And what that facilitated us to do is we have a lot of global thought leaders in our institution. We got together, and we asked ourselves the Richard Cormack: How can we use our expertise, our technology, and our knowledge to make a difference for cancer patients in this COVID period? And we rapidly established some research protocols. I won't go through all of them, but I'll give you a couple of examples.

So what is the immune response of cancer patients on chemo to COVID? And how can we use that information to safely deliver treatments? Over a thousand-patient study. Several hundred in it already. Collaboration with the Crick, who are absolutely major in immunology. And then I established a liquid biopsy diagnostic protocol. So we have huge strengths in liquid biopsies, detecting tiny quantities of cancer in the blood. We have the technology. We're running loads of clinical trials. And we had a problem with diagnostics. And we needed patients to access diagnosis in order to start treatment. So we've started that in the pilot phase, and that's been extremely helpful but also really informative to how we might actually do that approach in routine practice in the future.

**Richard Cormack:** Cancer, turning back to the kind of disease and the strides that people are making, you and your colleagues are making, I mean, unfortunately, it's something that continues

to impact so many of us. As you've said, you know, there have been great strides that have been made both in terms of treatment and research. You know, what are the other breakthrough treatments that you're seeing at the moment? And kind of where do you kind of have the most optimism?

**Dr. Naureen Starling:** So I think, I mean, the two main areas have been around, in my view, precision medicine across all cancers. So, you know, bowel cancer is not just one disease. And no two patients are actually the same in their makeup of the cancer. And it's about trying to A) understand that and B) exploit it therapeutically. And there have been huge strides in that. So I think the precision environment globally and in the UK particularly has really accelerated.

Say, for precision medicine you need technologies, precision tools to be able to identify these people. And then you need the treatments to successfully exploit the things that you find. So I think that has really changed in the last decade or so.

You know, if you think back to the sequencing of the human genome, that took years and billions of dollars to sequence the first human genome. We can now sequence the patient's cancer genome for at cost probably under 1,000 pounds in a few days. That is extraordinary. And I think that has really in the last few years accelerated the field of precision medicine.

So to give you an example in my area in bowel cancer, there are different groups of patients. There is a group of patients, 10%, whose tumors have a switch on. The [UNINTEL] mutation. It's also a mutation seen in melanoma. Now, we can identify these patients. They don't do as well as other bowel cancer patients. But the field moved quickly to find targeted treatments for those group of patients.

The regulators have approved a number of targeted combinations for that group of patients and really satisfyingly nice within the UK, just approved that combination for UCLH just a few weeks ago after an initial rejection. We campaigned, turned the decision around. And that's brilliant for that group of patients.

There is also a group of patients in bowel cancer, 4%. So you may think, oh, that's not that many, but bowel cancer is the fourth most common cancer in the world. 4% is a lot of patients whose tumors have a different defect. Something called mismatched repair deficiency. Their tumors are really shining

to the immune system and lots of mutations. And immunotherapy really works in those patients. We've now seen a trial reported recently where we may replace chemotherapy as the first treatment for patients presenting with advanced bowel cancer with that abnormality. That's a major breakthrough. The regulators are currently looking at it. And NICE will be looking at that early next year for whether we can use that in ULHS. I hope so. I think the data stack up.

That again is an immunotherapy approach but leveraging a precision medicine approach.

**Richard Cormack:** Right. One of the big challenges -- and you touched on this in terms of the impact of COVID -- is early diagnosis. Perhaps you can talk about that and kind of why are we not better at it? And how can we get better?

**Dr. Naureen Starling:** So I think it's multifactorial. I think it's around the health care system and how it's organized in terms of getting people quickly through a symptoms diagnosis and treated. I think it's around health behaviors. A number of patients in my clinic have said, "Do you know what? I actually did have these symptoms for months and months, but I just thought it probably won't be anything." And then there's something around the tests that we can deploy.

So in terms of early detection, screening of an asymptomatic population is a very challenging thing, both from, you know, the tests that you can deploy and the resource structure and utilization. I think there are also several difficult-to-diagnose cancers at an early level. Pancreatic cancer, I mentioned that earlier. Gastric cancers. Some head and neck tumors.

So it's probably a conglomeration of all of those things. Now in the Oak Cancer Center [sp?], we aim to have a whole floor designated to early detection but integrated with research. So we'll ask every patient to be a research patient in terms of sampling and understanding what tests can be developed. Now, you may have heard, we argue probably you will have heard in the news last week, it was a very big deal, the UK government have entered a partnership with Grail [sp?], who have designed a liquid biopsy test. Going back to liquid biopsies, detecting tiny fragments of cancer in the blood circulation. Their test is unique in that a component of the test, a methylation component, that can identify where that cancer has come from, which tissue. So in theory, it could identify, pick up 50

different cancers. Not all cancers. Prostate cancer, for instance, is not on there.

And I think that's extremely bold and ambitious for a health care system to do that. They're piloting this in 165,000 NHS patients. If successful, they'll roll that out to a million patients. And here we therefore maybe have the start of a diagnostic test that is actually easy, is more palatable to patients than some of the things we offer and could be rolled out more easily. Obviously we need to see what the data show, but, you know, I think we are on the cusp of a major change.

**Richard Cormack:** Right. I'd like to thank you for joining us today, for taking the time to share so much about your critical work that you're doing for all of us. Thank you, Naureen.

**Dr. Naureen Starling:** Thank you. Thanks, Richard. Thanks, all.

*any errors in the transcript.*