# Evolving Treatment Paradigm of Multiple Myeloma

In the past decade, the FDA has approved 13 new agents and 29 treatments for multiple myeloma, which have transformed the treatment paradigm for patients. The expanded treatment options have resulted in significantly improved outcomes. Two decades ago, the median survival was approximately 3 years, and now it is 8 to 10 years and can be even longer for many patients.

We are discussing the latest trends in multiple myeloma treatments and the next frontiers with Dr. Sikander Ailawadhi of Mayo Clinic, Anne Quinn Young of MMRF, Brian McMahon of SparkCures and Jennifer Ahlstrom of Myeloma Crowd Foundation.

**Full Transcript:**

**Priya Menon:** Hello, and welcome to CureTalks. This is Priya Menon, your host. Today's show is part of our Innovative Series where we discuss breakthrough treatments and research. The topic for today's discussion is the Evolving Treatment Paradigm of Multiple Myeloma, and on the panel our Dr Sikander Ailawadhi, Oncologist for Mayo Clinic, Anne Quinn Young, Chief Mission Officer of the MMRF, Brian McMahon, Founder/CEO SparkCures and patient expert Jennifer Ahlstrom, Founder HealthTree Foundation. Welcome to CureTalks everyone.

**Dr Sikander Ailawadhi:** Thank you.

**Priya Menon:** In the past decade, the FDA has approved 30 new agents and 29 treatments for multiple myeloma, which have transformed the treatment paradigm for patients. We have BCMAs, antibody drug conjugates, CAR-T cells therapies, bispecific therapies and I think we have a lot of ground to cover today. So, the goal is just to get some different perspectives. I'll start with you Dr. Ailawadhi. It has been exciting few years for myeloma as we all know with CAR-T also added to the myeloma treatment options. What do you predict will be the change in treatment scenario with this addition?

**Dr Sikander Ailawadhi:** Priya, thanks a lot for hosting this and thanks for all for the questions. And I'm glad to meet Jenny and Brian and Ann on the call. So, glad to connect with everybody again. So, I think you pointed out exactly correctly that this is a very exciting time. It's exciting for a physician, a clinician like me, who spoke at the myeloma treatment because I have more often discussed with my patients, and I have more often sequence therapy or try to plan something. It's also exciting for the researcher in me to be able to participate in these clinical trials and when suddenly even a phase I, gives an MRD negative response to a patient, who's had an auto transport, an Allo transplant etc. You cannot imagine how happy not only the patient is, the physician is but even the research staff who's dealing with that patient, that literally we can see that spark in everybody's eyes. And then above all, above everything else, I think it's the I hesitate to use the term exciting because unfortunately for a patient who's living with the diagnosis, I don't think that term applies but it's an optimistic time for that patient because they suddenly have more options, they can go to. So, I think if your question was, how do you see or what is the prediction or where is the field going, etc.

**Priya Menon:** Yeah.

**Dr Sikander Ailawadhi:** I personally feel that if we were to use a term of immunotherapy for multiple myeloma, I believe that era started potentially a year and a half, two years ago. And that area has a exploded, that area has suddenly this whole concept of T cell engager , CAR-T, other kinds of immune

mechanisms modulating the microenvironment, this sleuth of different mechanisms that are coming up, those different classes of drugs, I think, for me, that is the excitement, the prediction, the path forward. We're not just talking about the second or the third, or the fourth drug in the same family. We're talking about unimaginable, exciting new families of drug. So, I think that is where the immunotherapy, the combinations of these drugs in relapsed refractory patients, the opportunity of using these drugs even early on and getting those patients time and again, that deep response, and I think a bigger focus on the survivor took with myeloma because as we treat the disease better, we're being able to hopefully give the better quality of life to that patient and bring them closer to their goal within their life.

**Priya Menon:** I would just say research point of view, I think a lot of exciting things happening. Very optimistic, Dr. Ailawadhi I'll be back with you. Like to hear from the rest before we actually start discussing, what else is going on with myeloma. So, Ann I see that you're the Mission Officer of the MMRF, could you just give us a little background as of what a Mission Officer does at the MMRF? And then, as I said, we'll get in the real discussion.

**Anne Quinn Young:** Sure. To be a Chief Mission officer of the MMRF it's an extraordinary honour. I've been with the organization coming up on 20 years. And so, all of the progress Dr. Ailawadhi alluded to recently I can look back and when I started, how patients were treated is so incredibly different today, prognosis was so different. it's just never exciting to get a myeloma diagnosis, but the unprecedented response rates and depth of response, it's incredible. And we too are very optimistic for patients moving forward. So as Chief Mission officer, it's really my responsibility to make sure that every single thing that we do at the MMRF is in line with our mission and that's to accelerate a cure for each and every patient with multiple myeloma and there are the obvious, Are we investing in the right research, are we doing the right trials, are we investing in developing datasets and interrogating those data sets and make them available to drive Precision medicine and cures for every patient. But it come down to everyday decisions where we always need to make sure that we have our mission in mind and we're putting the patient at the center.

**Priya Menon:** Ann, can you also talk a little bit more about MMRF strategic priorities? I know we have been talking about patient centric solutions.

**Anne Quinn Young:** As I mentioned from the very beginning, when our founder Kathy Giusti, who is a multiple myeloma patient, and her sister started the organization. Our mission has never changed, how we go about achieving that mission has evolved tremendously as we as an organization have grown and evolved. And as a treatment landscape has evolved and changed quite honestly, very, very, very dramatically. How we look at our work right now is really in three different pillars; one is accelerating new treatments for patients. And that's because the disease is still largely incurable. We want to make sure that there's as many new treatment options out there, so, when a patient does relapse from a treatment, the next treatment is there. The second focus is really on driving more personalized approaches, Precision medicine. So, we generate data, we share that data, we analyze that data so that we understand how to use all these treatments that are currently available as well as those that are emerging. With all of the options that you heard that you mentioned Priya in the beginning that are available. There are so many different combinations. So many different ways to sequence these therapies and then when you couple that with the different patient types, whether it's based on genomics or new profiles, or anything else. There's so many different options and you really need a lot of data to make sense of that. And then the third piece is with all of these advances, all these new treatments, all these new trials we want to make sure that patients and the entire community are aware of them that they're educated and can optimize their own outcomes. This means knowing what research opportunities are available. So that again, any patient has an opportunity to participate but then also understanding all the new treatments that are available ones that might be right for them and not just limited to patients, who may be treated at large academic centers with myeloma specialist, but even patients in the community them in their doctors and their caregivers. Again, understanding what options are available to them to best optimize the outcome.

**Priya Menon:** Ann, I'll be back for some more details that MMRF is doing. Moving on to Jenny. Jenny, hi, I know, you are a patient advocate, and I should say patient expert and founder of HealthTree and myeloma

crowd. How have you seen in over the period of your care, how have you seen the care evolving for people living with myeloma?

**Anne Quinn Young:** I think as I said before a lot of different new options, whole classes of drugs that weren't available before, I was diagnosed in 2010 and I chose tandem transplant just because there was nothing. You said the word cure in that time period you're kind of mocked or no expert was talking about that word and you hear them talking about that word now. So, I selected that clinical trial, just recently went through a CAR-T trial, I did that very intentionally because I wanted to take advantage of some of these newer technologies that Dr. Ailawadhi said are making such significant advancements. And as a patient, I saw a lot of gaps during the course of my care which is why I created the HealthTree Foundation. _____ and to share their myeloma story. So, we can look at these new therapies and the data of these new therapies and say, what is the best at Frontline therapy for a particular kind of patient in the real world, what's truly happening? So, I see a lot of things evolved not just the treatments, which are very exciting but we're able to apply technology also to some of these problems that really haven't been done in the advocacy before and help accelerate that cure.

**Jennifer Ahlstrom:** Thank you. Thank you, Jenny. Moving on to Brian. Brian been a myeloma care giver and caregiver for many other cancers also, and I believe the gap in information and access to clinical trials had to come up with SparkCures. Can you talk a little bit more about how folks can find trials, what SparkCure does, and I like to know how far you track your trials, do you track people getting recruited as well? Be great to hear about that.

**Brian McMahon:** Yeah, so this really all started with my mom back in 2005. And I know I've shared the story publicly before, but it is a brief intro to this. My mom was diagnosed in 2005, which is a lifetime ago in the scheme of multiple myeloma. I mean, to put this into perspective, we're talking about CAR-Ts and bispecifics and monoclonal antibodies, none of those things existed in 2005, maybe daratumumab in some clinical trials, really early. My mom was diagnosed before revlimid was approved as an FDA therapy for myeloma to put that perspective. And the difference is that when my mom was diagnosed they give her a really poor prognosis, right. They didn't expect her to live a month even with treatment. She was sent home on a Velcade-Prednisone therapy, right. That was her first line. And the difference is my mom was 30 plus year oncology nurse who at the time was working for Amgen, right. So, not only did she have the clinical expertise, but she had the role that comes with working in a large Pharma company. Within two weeks, she had found a clinical trial, that was a thousand miles away from our home. So, this wasn't something nearby at the University of Arkansas and as much like Jenny, she underwent a tandem transplant. She was part of the total therapy III protocol in Arkansas. And the difference there is my mom end up living with her disease for about two years. And I would say it wasn't the outcome that we wanted. But when you're given a month and you get two years, you really understand and see the importance of what clinical research is bringing. And you see that the only reason these new drugs that we have CAR-Ts and bispecifics coming to Clinic is because of patients, who are participating in research and helping to push that forward and researchers and pharma companies and advocacy groups, right. This is a community effort to advance this so we can find that cure. And I think the point of starting SparkCures was that in a ten-year period, I was a cancer caregiver four at a times. My mom was the only one to go into a clinical trial, right. And there are stories that I can share anecdotally about the trials, and tribulations of going through that. But, we started SparkCures with a thought that in the promise that you shouldn't have to be a 30-plus, oncology nurse or working, a large pharmaceutical company in order to navigate your clinic trial options. And that's what we've been doing for the past seven and a half years.

**Priya Menon:** Thanks. Thanks. We know too well how difficult it is to get the right trial, be found eligible for that and then get enrolled. So, thanks Brian. Dr. Ailawadhi circling back to you. I know you talked about immunotherapies, having exploded it and having so many different types of drugs now. Could you also talk about the scope of Radio Therapeutics, which I think you're involved with, you are working on? And we'll also like to hear about the CLR 131 with some of the latest results. That would be great.

**Dr Sikander Ailawadhi:** Priya, thanks for that question. So, as we talk about these different or unique

classes of drugs, Radio Therapeutics are not something that are new to the area of cancer in heme-malignancies there have been prior radio isotopes, that are being used and there are radio isotopes that are used for example, in prostate cancer, some of the other malignancies. So, in similar light Radio Therapeutic are the unique class at least for myeloma because we have not had Radio Therapeutic previously. Now, what is the Radio Therapeutic? Just for those who are our listeners is basically a drug with a tiny amount of radiation attached to it. And this radiation would be given as an medication, as an IV medical for example, and then that would go around to meet the target that it is against, so whatever is that “drug” that will seek the target and then deliver that radiation at that target and try to kill that cell. We know that radiation is very active in myeloma. We use radiation time and again, for different reasons. So, if there was a drug that could speak plasma cells and be able to deliver radiation there. That would be a desirable treatment option. That’s the whole premise. So, at Mayo Clinic over here in Jacksonville, Florida, where I work and lead our myeloma group, we’ve been involved with one that Radiopharmaceutical or Radio Therapeutic for myeloma for quite some time. It is called CLR I-131. And over the few years that we’ve been involved with the drug has made its way through a lot of different iterations and whether it be given as 1 dose and or fractionated dose. And now, the way this trial is set up is that it’s getting people two sort of fractionated or flip dose initially and several weeks later, people get another two doses. But it’s basically the total amount of radiation being given in split apart so that it’s less toxic, but hopefully more beneficial. You can almost imagine as our bispecific antibodies for myeloma came about, they were initially just one regular dose. But now, most of bispecific is the step-up dose to be able to give it more safely. Similarly, the Radio Therapeutic is given in split fractionated dose to be able to get more benefit. Our experience has been, we at Florida has probably treated more patients, than anybody else because we’ve been involved since the beginning in different dose levels, different diagnosis, whether it’s myeloma, Waldenstrom’s, different kinds of lymphomas. So, what my experience has been that the way the study is set up is a little unique because it gives the people treatment, follows them to a certain period of time when the patient has gotten over all the safety concerns from the drug, if any. And then at that point that we have assessed what’s the response rate and so far majority of the patients, I can tell you who’ve gone on this drug follow a period of several months have had stable disease or better, some even have responded but stable disease are better and we have frequently used this. But I just had a discussion with the patient earlier today about this. We have frequently used this as a bridge when the patient is looking for a treatment option where they could come to a center, get the clinical trial treatment, and then go back to their home and keep getting a lot of the standard of care close to home and hopefully have disease stabilized. The things that I keep in mind when I talk to my patients about this is that there is an option where they get just that radiopharmaceutical as an IV treatment in four different time points spread over several weeks, and in between the patient is actually able to go back to their local physicians if getting monitored with labs by the way, there is no treatment in between. It is just those four isolated doses of the radiopharmaceutical, there is no dexamethasone, nothing in between and the patient frequently just follows for the local doctors that how conveniently the clinical trial is written. Because there’s somebody as Brian was mentioning, Brian you were mentioning about your mother that she was able to identify a trial but that was miles away. How many patients have the resources or maybe they can come once or twice, but if he starting hey, you’re going to come every week, how is that even possible. How is that person going to live away from their home without their caregiver, support group. How are they going to do that? Those are the other positives about the trial. What we’ve seen is that we are at a point now that the dose is defined, and it’s not like a dose escalates, whether it will work or not. Dose is defined. We expect that after the patient gets first two doses almost like clockwork. Two weeks later the count go down. That will probably stay down for about three weeks or so where the patient may require some growth back or transfusion support and then the count come up. In majority of patients that disease goes down and stays down for a certain period of time. That is given me an opportunity to find them that plot on CAR-T or find them that plot on the bispecific etc other treatments. For us it worked out as an excellent bridge to the next thing.

**Priya Menon:** So, Dr. Ailawadhi who is the target patient population here? Who would be eligible for receiving those?

**Dr Sikander Ailawadhi:** The way the clinical trial is written, patients are broadly eligible. And in fact, I should point out, I don’t want patients to get a false hope around it but the sponsor has actually allowed some of the

non secretory patients to also get onto the trial. That is a subset of people who do not have any measurable disease in their blood or urine. And unfortunately, the only way of testing is either repeated Imaging with PET scans etc or bone marrow biopsies. But every now and then we have been able to get approval to even get non secretory patients because we have seen that they also benefit that is just the unique thing. I can't say that every non secretory person, can go on. But every time we have a patient, we make a request, we evaluate and if the company feels that they have the bandwidth to accommodate a non- secretory person in the trial then probably they have done that. So, in my mind, I've used this for patients who have gone through some of the additional lines of legitimate therapy, the proteasome Inhibitors, the immunomodulators, the monoclonal antibodies, maybe even CAR-T. We have now had patients who had prior CAR-T, have disease progression, but frankly, BCMA targeting therapies, CAR-Ts or bispecifics, they are able to give long term responses to a subset of patients, but a lot of other patients still progress after that. So, we need options. So, we have used this for a broad, different variety of patients in the relapse/refractory settings, who have typically gone to the first three, four lines of therapy and have gone through most of the legitimate treatment options that are available.

**Priya Menon:** Thank you. Thank you, Dr. Ailawadhi.

**Brian McMahon:** Priya, can I jump in on really quick. I just wanted to, I think there's two points Dr. Ailawadhi made, I just want to make sure we reiterate and one of those is the quality of life and logistical load of traveling for a trial, which is just so it can't be understood the importance of this. So, when you're looking, even some of the bispecifics, it might be once a week, it might be once in 2 weeks, they're ones that are once every 3 weeks and even some of the trials, it depends on the cohort. So, some of the cohort, maybe weekly, some maybe once every two weeks, right? And I think it changes the conversation and when you are saying there is a limited duration of therapies such as CAR-T or such as the CLR 131. All of a sudden, the thought of traveling down to Mayo Jacksonville from Rochester or from the middle of the country, maybe a little bit more tenable, you might be able to do that. Right? So, I think understanding what the expectations of the trial, what that looks like and what the treatment requirements are is just so critically important. It is number one, and the second thing is, it's always helpful to ask we know that non secretory is a hard exclusion for a lot of trials. It is a hurdle to get over but not all of them, right? And even as Dr. Ailawadhi is saying here, it's not a give-in. Right? But we love it when sponsors are willing to at least look and take physician input from the physcian and say is this a safe and prudent choice for us to go on as a non-secretary patient because what else do we left with. Even some of the expanded access programs don't allow for non secretary patients, which to me is mind-boggling and then anyways, we have no other options, but you're non secretary so we can't give you this. That's another conversation and we can get into that but I think be an advocate, ask those questions, have your doctor talk to the Pharma company. Some are willing to bend, others aren't but squeaky wheel gets the grease essentially. I just want to make sure that those two points are sort of reiterated. So, thank you.

**Jennifer Ahlstrom:** Yeah, I kind of make a point too. So, Dr. Ailawadhi does a lot of disparities work and really did a lot of work trying to understand at his Clinic why someone would join a clinical trial. He put together his own questionnaire, but then he shared that questionnaire with us, we put it into our,HealthTree Curehub platform and then we socialized it with all the myeloma patients in that platform to better understand what the issues are of joining clinical trials? Is it travel, is it free dosing, is it frequency, is it side effect profiles? (voice breaks) _____ our responses (voice breaks) _____ to understand what are the issues for a clinical trial development? You think about all the new clinical trials that want to be more distributed or those opportunities that could exist with better technology and really open up the platforms of these clinical trials to different people who may not be able to do all this trouble or have barriers for certain things. So, I just want to applaud his efforts in trying to understand the issues, and it was a privilege to be able to help him find the answers to those using the HealthTree database.

**Priya Menon:** Thank you.

**Anne Quinn Young:** Can I make one more comment here.

**Priya Menon:** Please.

**Anne Quinn Young:** I mean those are on a lot of different points that were made multiple myeloma as everyone on this webinar knows and hopefully people watching it, it does predominantly affect a number of traditionally underserved patients, who for a number of reasons, can't travel whether it is financial, whether it is physical, there are many different reasons. And we are also committed to making sure that we're taking away some of those barriers for patients as well. And some of those have been talked about already financial, one commitment that we're making a strategic plan is to make sure that financial barriers are not a reason for participating in clinical trials and even some of the bispecifics or CAR-T where patients are hospitalized, forget about the traditional childcare, transportation, but if someone's an hourly worker that becomes a lot more difficult both for the trial but even when these treatments are FDA-approved. And another piece related to the non-secretory is eligibility criteria and the traditional eligibility criteria for multiple myeloma tends to exclude a lot of the patients who probably could benefit most from the clinical trials. Those that have significant comorbidities and then even in terms of standard lab values, they don't necessarily apply to all of the patient populations. So, this is another area where we as an organization want to work with the entire community to say, can we look at the eligibility criteria for trials will be convening something in the fall would love every single person on this line to be part of that. And then get buy-in from the community and hopefully take that forward so that trials can be much more inclusive. It drives me crazy when I see five percent of cancer patients participate well part of that is they're just not eligible, it's not that they don't want to or there are the barriers that the Jenny mentioned but the straight up they're just not eligible to be part of the trials, even if they could get there and there were no financial barriers. So, these are things that we feel very strongly about. And again, it's going to take the entire community working together. It's no one single entity is going to solve this.

**Priya Menon:** Thank you, Ann. Thank you for that.

**Brian McMahon:** Priya, if you don't mind. Dr. Ailawadhi, I'm curious. So that was a great question. And is there two-fold, one Jenny, your internet was breaking up a little bit. So, I don't know if you shared this but what was the big takeaway from the survey? What was what was some of the biggest things that you learn one? And two to Ann's point, what are the biggest exclusion criteria that we're seeing especially from a minority patient population. Is it measurable disease, is it kidney, like, what are their lab values are excluding on that side? Can you briefly touch on that?

**Dr Sikander Ailawadhi:** Brian, thanks a lot for that question. Because I hadss raise my hand because I wanted to touch upon a few things, but I didn't want to kind of know if Priya had time to ask all the things that I wanting to. So, I'll quickly talk about a few things, so yes, external collaboration with HealthTree, by the way, in my mind, this is the way to do real world research, rather than just looking at databases where things are missing. HealthTree gave us, for example a platform, to be able to run that survey among specifically myeloma patient. I'll be forthcoming and say that that particular analysis out of the myeloma patient from HealthTree. We have not been able to complete that analysis. Yes, because you can imagine doing the statistical analysis on the survey, which is a 55 question survey, breaking it into five different domains and then running an analysis and doing it according to patient's criteria age, demographic, etc quite complicated but not been able to finalize that analysis. But I'll share with you that we did analyze the first 250 patients at Mayo Clinic. This was a lot of different kinds of cancers, not specifically myeloma. Myeloma was a big part of it and the survey is focused and we created this survey with our Mayo Clinic Survey Research Center. So validated questions, keeping in mind what service, how the language should be, if non-leading etc. And the survey is focused on five different domains. It does talk about bias and fear of research and fear of pharma, awareness etc. And the commitment to the study was that we're going to initially we said we're going to enroll 500 patients. We said that at least one hundred will be African Americans and at least 100 will be Hispanic because we don't want the minorities and underserved to be kind of diluted out in the final analysis. So, the first analysis we ran was about 250 patients when we hit the half mark and those 45 are African-Americans, 45 are Hispanics and the rest were white. And what we found was that African Americans had a statistically significant lower awareness of clinical trials. That was the one thing that came up different in our initial analysis. That portion, that 500 people analysis is being done. But to

qualify that think of it this way. These are all patients who are coming to Mayo Clinic, they are already meeting a certain criteria that they have come to Mayo where about 60 to 70 percent of our patients may be coming from distances. So, they have some means, they have thought about, they are coming to a large centre. These are all patients who are new to Mayo. We didn't want to buy it by the information, we give to patients. So, these are those who were new to Mayo and still African-Americans had a significantly lower awareness across. So that is just setting the stage. But we are running those analysis, we're hoping that at least some updated analysis can be brought over that. And the second part of the question which Ann you raised, and I didn't touch upon it earlier, but Priya it is important for the whole of our listener pool to be able to realize, and estimate I do a lot of work with health disparities and within that clinical trials, is a big focus of my work, but it's important for everybody to realize just like Ann said, a lot of times patients who are traditionally underrepresented in trials that trials are actually set up in a way, the inclusion criteria is setup in a way against them just like what I have mentioned. So, we publish the paper now and I believe 2014 and then update that was 2018 is that I think, where African-Americans are more likely to have more anemia, more kidney dysfunction, more need for dialysis, and more hypercalcemia, and the traditional myeloma defining event at the time of diagnosis. The one thing that African-Americans have lesser is fracture because they are genetically stronger with higher bone density. So, with that whole background, we also know that African-Americans tend to have lower neutrophil levels  as a race nothing to do with myeloma as a race, lower neutrophil levels, so it's easier to exclude out of trail. So, with that backdrop, and I'm glad that MMRF is looking into it and I'd be glad to participate and help in any way. So, we have a forthcoming newly diagnosed or randomized phase III, Cooperative group, clinical trial coming out of SWOG, and I'm prepared for that and I have a couple of very good coaches there who we are writing that protocol. And the idea is this is going to be a 500-page clinical trials supported by NCI, but we are challenging this paradigm. We will allow patients to the hemoglobin, not eight but seven would be the limit. We will allow patients to go on not with the ANC or the absolute neutrophil count of 1, but 0.75. We will allow actually transfusions and growth factors to get onto the trials because the bottom line is, well, if you have enough disease, that you need to be treated it doesn't make sense that the disease is the problem and you don't want the patient on. And two nights ago, I think I was on a forum which was a pharmaceutical company run forum. And I made a huge plea to that particular company. I said guys, I know this is putting your drug in an unsafe zone to be giving your drug to patients who have poor kidney function, poor count etc, but please whatever you feel there is a possibility make that point. So, for example, in that trail currently as it is written, every patient will go on irrespective of kidney function even dialysis patients. But there is a lot of discussion going back and forth where the sponsor or the supporter of sponsors and Pi with the support of the studies saying that, well, we just feel a little uncomfortable because the safety in dialysis patient has not been defined and I get that. But short of dialysis is most likely, every kidney function will be allowed to go on and we're making an attempt. And frankly, we will track if this helped bring in more minority. So hopefully it'll come full circle, but I'm glad that we are talking about all of this to you.

**Anne Quinn Young:** Is the protocol IRB approved and it is moving forward with that?

**Dr Sikander Ailawadhi:** Not yet IRB approved, but NCI has reviewed it and NCI is actually given a green light to move forward, with that concept with those inclusion criteria. The myeloma steering committee, I would say, kudos to the myeloma community where the myeloma steering committee at NCI has actually reviewed those and has given us the go-ahead to do that. So, the protocol is currently being developed. And we're hoping that by quarter three of this year that newly and that is also I could add is specifically for patients who are frail, intermediate fit, elderly and the goal is well these are the patients who we don't study, but these are the patients who we see in clinic. So, it'll be a trial newly diagnosed for frail and intermediate fit, elderly patients, previously passed but ineligible person, and it will allow a lot of kidney dysfunction and allow a lot of lower count, because bottom line is trial or no trial I'm the doctor and that's my patient, I have to treat them. Is it possible for me to treat them on file, trying to make more real world studies?

**Anne Quinn Young:** And I think I'll just take one. I mean, again, it's going to take the community. But once there's one trial…

**Dr Sikander Ailawadhi:** You got to start somewhere.

**Anne Quinn Young:** We can influence the rest. There aren't too many hard-and-fast mandates or regulations, even FDA, doesn't mandate that the trials look like the population of the disease, that there are certain groups that are represented. But the more I think we, as a community, can unite and really push for these types of things. I do think change is possible.

**Priya Menon:** Thank you, I think that was quite a good discussion on trials and equity. Ann, I know MMRF is doing a lot on this. Also why don't we just educate our listeners on the multi-pronged approach that MMRF has towards it to Advanced Precision medicine, touch upon CureCloud, MyDRUG.

**Anne Quinn Young:** Sure, absolutely. So, it's long been known for many, many years, even when we didn't have to say the technology, we have today that myeloma is a heterogeneous disease. It's not characterized by a single mutation like some other cancers are. So, that being uncommon, it's not like there's enough patients at any one center to really understand the diversity of the disease and how best to treat those different patients. So, we've had a commitment. I think we launched our Tissue Bank back in 2004 to creating a central resource of a critical mass of patients and data to help the entire research community start to make sense of multiple myeloma. Our biggest effort to date as it comes to say that launched in 2011 where we enrolled 1100 newly diagnosed untreated patients. It took 76 different sites in four different countries, but we follow those patients, collecting their clinical data, doing DNA and RNA sequencing on three different platforms for at least eight years. So, enrollment took four years. We still have about half those patients enrolled in the study and continue to collect that data. It's taught us some really important findings. We've identified new targets. We've taken them into MyDRUG that I'll mention next. It's also helped us better understand risk. The whole concept of double hit, missing both copies of p53 versus just one which was only FISH can really differentiate between the two now with genomic sequencing we can and really understand who's at higher risk for the importance of 1q amplification, which has been replicated in other studies as well. But just how important that is as a risk factor, Compass has been really helpful. And again, helping the community understand that. Then we did take findings from Compass and we created a platform trial called MyDRUG. So, there's six different arms and patients are assigned to an arm based on their specific genomic alteration. About 50% of patients, don't have a genomic alteration and been put in now, three different arms that they're put in. But what's been exciting so far as we've seen in one of the arm's we've seen some clinical benefit and last year we had presented information on Cobimetinib and we've expanded our cohort where there's a post at ASH too and will continue to follow those patients again. What this has meant is opening up treatment options for patients who may have run out of treatment options. All the treatments in MyDRUG are FDA-approved, oral treatments for other cancer. So, they're commercially available and then our other effort into space is CureCloud and newer effort. And it's also a longitudinal clinical genomic, study like Compass, but it's different in that we can enroll patients anywhere. You don't need to be seen at a specific center. It's still an IRB approved research protocol designed to answer the question of what patients should receive what treatments and what combinations and what sequence. But again, you can enroll online. Patients sign a waiver so that they contribute key details from their electronic medical record. They don't need to complete a lengthy case report form and then in an attempt to can we move beyond at some point bone marrow biopsies, we have a liquid biopsy, means we take a blood sample and then sequence out on a panel of 70 genes that are commonly seen in multiple myeloma. How this is different is we don't have the deep sequencing information, but we have a wealth of clinical information. We have clinical information going, all the way back to when patients were diagnosed. So even though patients are enrolling at different points, in their journey. We have a lot, we have longitudinal pictures now of more than 800 patients and similar with Compass, we are committed to making that data publicly available to researchers as well, again to continue the field and generate hypotheses, that could drive Precision medicine.

**Anne Quinn Young:** One point to tell a couple things together too. So, there's clinical trials which are very important, but there's also the observational research that I mentioned as well, which is Compass, which is CureCloud. And what we're doing now is CureCloud is we made a direct patient, always be direct patient, but now we're adding a hybrid model where we're going through sites. And what happened? Why we're doing that is, we're working with sites and we've worked with Compass and CureCloud, who have a successful track record in enrolling a diverse set of patient. The patients that look like the real world facing

myeloma, but what we're finding is in this direct to patient model. They're not necessarily enrolling in the trial. So, then we had to go back to what the barriers are and it's simple as the doctor tells a patient and this is in particular, we're trying to make sure that we have enough, black patients enrolled as well about the trial they are excited and then nothing happens. So, to take away that the burden on the patient, to remember to go home, to log on, to sign the consent or for some patients it may be as simple they don't have access to steady Wi-Fi. So, we're working with the sites and we will be arming them with the technology to make it possible. And funny enough, as a direct to patient initiative, some sites want the paper consent. So, it's a funny thing where you combine technology and making this available to everyone, to going back to Memphis to say, not everyone has access to technology or comfortable with it. So, how do we make this as easy as possible for patients because again trials are one thing, but if we're not enrolling a diverse set of patients in these observational studies we are never going to understand where you have differences in outcomes, what's biology, what's access. Because you need that representation from all different parties in the studies. And they're still friction or hesitation or lack of knowledge about enrolling in even those kinds of studies forget about Interventional clinical trial.

**Priya Menon:** Thank you Ann. Just want to be mindful of everybody's time. One last question before we wrap up. What next for myeloma Dr. Ailawadhi?

**Dr Sikander Ailawadhi:** Sure. So, Priya this is to summarize. I think, what's next I feel because of all of this effort that is being done by patients, advocacies, pharma, regulatory, Institutional, clinicians. I think, what's next is, I'm hopeful that we will see a larger, broader access to clinical trials and novel treatment for everybody including our traditionally underserved patients. I'm very hopeful that will happen, and I think what's next is, what will happen is, newer classes of drugs will come by, but I'm hopeful or what I want happens is that we get a slightly better understanding of how to sequence the right drug for the right patient, at the right time and that's where I think efforts from those like MMRF and HealthTree and SparkCures will also help us figure out. I'm a clinician, I have a patient which drug, which regimen is right for my patient to use at this point. So that kind of precision medicine focus is where I want the field to go, but what's next is, lots of different promising options that will become available and broader clinical trial enrolment which I'm hopeful will happen with time.

**Priya Menon:** Thank you, Dr. Ailawadhi. Ann, your turn next. So, how is MMRF doing to ….?

**Anne Quinn Young:** I think Dr. Ailawadhi said it best. I mean I said at the beginning we talked about this at the beginning. There's unprecedented hope and optimism and potential transformation in the field right now. It would be a complete travesty if only certain patients benefited from those breakthroughs. So, it's a competent on all of us to make sure that again all patients have access to the trials, and ultimately to the treatment. And then the data from all of us is made available. And then, how do we better collaborate to answer those questions of precision medicine, where based on all different characteristics of a patient we can tell a patient and their doctor, okay, here's the right combination, in this order, based on your genomics, immuno profile, etc. That's the future, and that's how we're going to get to cures.

**Priya Menon:** Thank you. And Jenny, I know HealthTree is doing a lot in terms of educating the community. What is next for you as an advocate?

**Jennifer Ahlstrom:** Well, it goes along with what has just been said. We think these things need to go faster. Research needs to be simultaneously faster. And that's why we built the HealthTree Curehub platform. So, we now have over 10,000 patients, who are participating in that portal. And probably what we can do is we worked with about team together (voice breaks)____ on specific research…..

**Priya Menon:** I think Jenny is getting cut off.

**Jennifer Ahlstrom:** Yeah, I don't know why my internet is… But we'll be opening the platform up to allow researchers like Dr. Ailawadhi to answer these research questions simultaneously, using real-world evidence. And we've asked some of these investigators, we just ran a survey, even what does cure mean to

myeloma patient and we were able to get 1500 responses in less than four weeks. And I asked the investigator how long will that have taken you? Oh, a year or maybe a year and a half and probably, at least a hundred thousand dollars to hire a research coordinator. Why? Like, it doesn't make any sense to how the expense and the time to answer simple questions like that. So, (voice breaks)___ headed use this (voice breaks) _____in better ways. It's just kind of ridiculous that we have to be, we can run IRB approved studies simultaneously in the platform and come to conclusions a lot faster. That's where I think things need to head.

**Priya Menon:** Thank you, Jenny. Brian any last message?

**Brian McMahon:** All that stuff was great. Yeah, I agree faster, I think and unprecedented hope and optimism think it's great, that great way to phrase that. I think that we need to raise awareness. I think if you're a patient, make sure you're seeing the specialist. I think the idea of these novel therapies going early and earlier into the lines of therapy. In fact, we're seeing trials with bispecifics and smoldering that are going to be coming up here. I mean, this is a really exciting all due respect time in terms of what we're seeing from the data standpoint and when patients going to be able to access this in their journey with myeloma. So, I think all that is really amazing. So, consider joining a research study, whether it's observational that it's just as helpful as its therapeutic or treatment-based trials, just help provide insights in this. It's the only way we're going to move forward with this and find that cure whether how it is defined, that's how it's going to happen. So, thank you.

**Priya Menon:** Thank you. What I find most exciting is patients stepping up and partnering with investigators, researchers towards this particular goal of finding more treatment, finding a cure. So, on that note, thanks everybody, thanks for everything that all of you are doing and thank you Dr. Ailawadhi and Jenny and Brian for joining me today on CureTalks. This talk will be available on our website. Have a good evening. Thank you, everyone.

Thank you.