Myeloma 2017 - Year in Review with MMRF

The MMRF is pioneering precision medicine initiatives in multiple myeloma. This would help match patients to the most effective therapies based on their genetics and other unique factors. We are talking to Anne Quinn Young of MMRF to review myeloma research initiatives at The MMRF, specifically cover The MMRF CoMMPass Study updates, MMRF Answer Fund program, clinical trials currently recruiting and opportunities that patients can explore to share their data and participate in research efforts to accelerate precision medicine.

Full Transcript:

Priya Menon: Good afternoon everyone and welcome to CureTalks. This is Priya Menon joining you from India and we are kick-starting 2018 with a discussion on multiple Myeloma. The Myeloma panel is led by Gary Peterson, Myeloma survivor and editor of myelomasurvival.com. And joining Gary on the panel are myeloma survivors and advocates Jack Aiello, Cynthia Chmielewski and Matt Goldman. Welcome to CureTalks.The featured expert on today's talk is Anne Quinn Young of the Multiple Myeloma Research Foundation. Anne, it's such a pleasure to have you with us again.

Anne Quinn Young: Thank you. Happy to be here.

Priya Menon: The MMRF is pioneering precision medicine initiatives in multiple myeloma.This would help match patients to the most effective therapies based on the genetics and other unique factors. Today Anne will share myeloma research initiatives at the MMRF, specifically cover the MMRF CoMMPass study updates, MMRF Answer Fund Program, clinical trials currently recruiting and opportunities that patients can explore to share their data and participate in research efforts to accelerate precision medicine. As always, we will be taking questions from our audience at the end of the discussion, do you send in your questions to priya@trialx.com or post it in the comments section on CureTalks.com or you may also press one on your telephone keypad and we can bring you on air to ask your question. With that, I will now hand it over to Gary to begin with the discussion. Gary you are on air.

Gary: Yes. Hello Anne Quinn Young. How are you? You need a few more names though. Anne is the senior vice president of marketing and communications at the MMRF, partially it's brand strategy and execution of marketing and communication efforts across all the channels. And most of all, what I said was that you happened to be for the patients, the face of the MMRF, people personally that we most often see at patient seminars and things like that. So we appreciate everything that you do and letting us know what efforts that you guys put forth for us. And so thank you very much. And, and welcome again. It's a pleasure to hear what a MMRF is doing to keep us alive. Well I'm hoping not to have that. Now that MMRF one of its key initiatives is a complex trial, and that's been in place for some time now, but could you please give us an update on the results of that trial today and what you believe as you look into your crystal ball, what will come out of this in the future?

Anne: Well, thank you Gary and Priya and Jack and Cindy and Matt. I honestly, I love being part of this and look forward to every year. It's a little scary how quickly the year goes by and all of a sudden, here you are again, but it's such a pleasure to do this with such old friends and, patients who are making such a difference in the lives for thousands and thousands of other patients that I've always so impressed by how well informed everyone all of you are. It's truly inspirational. So to answer Gary's question, for those of you listening on the line who aren't familiar with the MMRF CoMMPass study – it's a study that we launched

back in 2011. And the goal, was at the time, and it's still is the goal to map out the different sub-types of Myeloma.

We all know, all the patients or the caregivers on the call know that Myeloma differs tremendously from patient to patient in terms of which treatments you respond to, the side effects, the symptoms, the complications, the duration of response to therapy. And what we really wanted to do with the availability of whole genome sequencing is to understand the disease at its deepest level and start to understand what those subtypes of patients maybe and how best to treat them. So we launched a very ambitious $40,000,000 study, to follow over a thousand patients longitudinally and that means, around eight years, to understand the course of their disease and really deeply profile, at key points. So the challenge in the beginning was to enroll these patients because we need a thousand patients prior to treatment. So there were a number of patients who had to have a repeat bone marrow done and we're so grateful that they raised their hand to be part of this. So we sequenced patients prior to the initiation of treatment, and then we sequenced them at each time that they relapsed as well and throughout our collecting clinical data. So by the time we closed enrollment in 2015, it took 76 centers in four countries to get us to that thousand., and actually 1,150 patients because we have a data sharing agreement with some Italian centers. So it's amazing.

I mean, it's such a tremendous resource. It's the largest genomics data set of any cancer. So breast kids, prostate cancer, all of these cancers that are so much has so many more patients. We have the largest genomics data set because we have three types of sequencing, not just on every patient but on every patient sample. So what we've learned so far is from a clinical level, we've helped validate answers to questions that are already, that are also being validated through larger randomized trials. Like a couple of years ago, it was obvious that being treated with three drugs versus two upfront led to a longer progression free survival. And again, it was pretty great for us to see because when this was presented at, the IFM Dana Farber study, presented similar data in a randomized trial. So we had real world evidence of this going on. They had a trial and indeed now the standard for most patients is three drugs versus two. Now, what the CoMMPass study will also help us understand when we interrogate the databases, are there patients who only need two, are there people who need two drugs, whether it's a proteasome inhibitor in a steroid or an inhibin in a steroid, and that obviously would save the patient toxicities, costs and all that. But those are the type of questions that we can ask another one that, the early data started to show confirm as well and similar data came out of the IFM GFCI study was that having a transplant earlier again, was better than waiting. Same question though with the three versus two. You know, the challenge in front of us is to interrogate the data to say OK, which patients really don't benefit from transplant.

So, don't go through all that a transplant requires you to do because you're not going to benefit versus you know, these patients that really should because they do, have a benefit. What we're starting to learn now, and we don't have real data to share yet, but as follow up continues, it start to answer the question around maintenance. Certainly the studies that have gone on or indicating treating until progression, but we'll be able to see through CoMMPass, start to see through CoMMPass. Are there patients who that's not necessary or are there patients who benefit more from a proteasome inhibitor versus an IMID. So a lot of the, so those are the really, I think easy to understand, are things that we've learned through CoMMPass, a lot of what's coming out.

Gary: So what is the genetic measures of gene expression profiling?

Anne: So it's whole genome sequencing, whole exome sequencing and RNA sequencing. So on every page, every event for every patient, we gather that data, that's what makes it the largest data set. So it's not the largest data set in terms of the number of patients, it's just the, I don't know what the size is. But when we, for example, put our data, the data available to the Genomic Data Commons, which had, I want to say like 30 different data from like 30 different cancers from the Cancer Genome Atlas program, we added 50% more data on there just with our one study in Myeloma. So you know, what we're primarily learning and just coming out of ASH, I'm there about 25 different abstracts and compass are, is primarily in the area of new targets and starting to understand possible mechanisms of resistance and response and a big area big focus on defining high risk patients because of the treatments available to newly diagnosed patients now,

thankfully most patients on CoMMPass haven't relapsed yet. So they are still in remission either following their first line therapy or first line therapy followed by transplant in most on maintenance. The patients who relapse in the first, with under two years, those are the patients we're really starting to learn from and starting to come up with some hypotheses in terms of what constitutes high risk. And indeed there have been a number of new targets found and also signatures that need to be validated that hopefully will allow us to better identify high risk patients because unfortunately the current ways to identify high risk patients aren't very predictive.

And even actually one of the most interesting things, I think useful things that have been found through CoMMPass and Gary kind of gets to your question about what was done in it. And we can only learn this through sequencing. So most in the call know that if you're a patient who said you, you have deletion of chromosome 17 p, that's bad. But what we learned through CoMMPass and, and really you need sequencing to do this, not FISH, is it has to be both copies of 17 p or PCD3 or gone. Jonathan Keith, who is a partner at CoMMPass, uses an analogy that I think is amazing. If PCD3 is a tumor suppressor gene, if you only cut, it's like a car. You cut out, you have two sets of brakes, the front of the back, you cut off the front, you can still stop the car, it may not stop quite as well, but you can still stop it. You cut off both. You're not, you're not stopping it. So you know what we've found, if you're missing only one copy, those patients do pretty much as well as other patients as you know. And so there is a group of deletion 17 p patients out there who have been told you're high risk who probably aren't. So what we need to do, and this kind of gets to the finally to the crystal ball question, is how do we start to take some of these learnings like that into practice so that sequencing is made, is validated and paid for and made more widely available so that patients have a better understanding, not only of their risk and prognosis, but also, as we start to better understand, targeted therapy which treatments are most likely to benefit from it. So that's the and then the other piece that we're also starting to look at is along the lines of the front line three versus two. Can we start looking at treatments for first relapse or second relapse relapse and are there, pathways that we may, is this data that we may want to share with insurers, for example, to help them understand, you know, the real world response, you know, it's not a randomized clinical trial, but can give some indication and perhaps justification for the coverage of these, these agents for patients.

Gary: Did the analysis come up with the best three drug combinations, for example? The reason I ask is I saw KRd just came out and said that they had a nine month improvement over Rd. But VRD versus RD had like a 13 month improvement. But that was with newly diagnosed patients. So it was a little confusing that under one condition nobody diagnose VRD shows improved progression free survival versus KRd versus the same thing in relapsed patients, you know, just the difference. So it is a little confusing.

Anne: You asked a good question. I pulled up the latest CoMMPass and that's not in there, but I do know the answer to the question. So in the CoMMPass data, as you can imagine, the most commonly used not only triplet with regimen was RVD and KRd because a lot of the, those 76 sites, are community and also you have to remember when it started back in 2011, the use of KRd up front with not widespread by any means. So I don't believe it's statistically significant, but the best outcome, at least from the data the last date I saw was KRd up front. But again, I don't think there are enough patients to make it statistically significant.

Gary: Ok. Thank you, one of the things, that I noticed, I was surprised to know from a business environment is that we generate all this data and it just goes for nought, yours is probably one of the first, if not the very first, close to being one of the first that have actually tried to capture that data. And recently I saw that…somebody at ASCO partnering with a company called CancerLinq and they were trying to mine data from 1,000,000 cancer patients and will CoMMPass be able to tie into this big data program?

Anne: So we have spoken to ASCO. The challenges, the big challenge here are really two fold, so a million cancer patients but a much smaller number of myeloma patients and the amount of genomic information is very limited is my understanding. So I would say more broadly, we are, I say for the past two or three years we've been in discussions with a number of different, you know, both centers and companies about sharing data and it's not that, not even that we would say, ok, you know, dump your data into our database, but if there are certain research questions that require more data, could we create a model where that data is, you

know, the data is pulled together in a, in a safe place where, again, we don't get full access to their data, but it's being combined with CoMMPass to answer some. I, we don't have any firm commitments. I think we're getting closer. I do think there are some academic centers who are talking more about data sharing and, in a public way because, often you'll hear centers talking about data sharing and it's really, with each other as opposed to the public. And again, our data, CoMMPass data is open to any non-profit researcher. So at an academic center the for profit is a little bit different who wants access to it. And I think I told this anecdote last year, but, if I didn't, this is one example of opening up it even beyond, medical researchers or PhD researchers in cancer, we opened up the data about a little over a year ago via this company called Top Coder who has all these like just get like data scientists across the board. All they do is crunch data. They're agnostic to where you, the kind of data it is to come up with model predictive models. And we put the question out there. It was a $30,000 award to say, can you come up with a predictive signature for patients who are, who are more likely to relapse within, x amount of time and the winner, the most predictive signature came from, a guy working in the forensics department of the Rio de Janeiro police department. So it, it, you know, where we're now working with Top Coder and this is also through Harvard business school to validate the data and with another data set. So there are places where there is data sharing going on and were appreciative because using just CoMMPass data alone and thankfully there aren't that many relapses. We don't know if this is just a numbers thing and in the real world it's not going to play out or when you put it with different data it's going to play out. So it's, I think bringing many others into the field is important, but we don't have the same, we're not governed by the same incentives that, for profit companies or academic centers are. So it's, and I'm not apologizing for them, but it's more challenging for them to open up their data when they're worried about publishing and IP and all that and we don't have those concerns.

Gary: You know, a boss of mine once said, he says you cannot manage that what you do not measure and I'm just so thankful that you guys are in the data and the answers are right there in the data, or will be there and I'm just paying for that now we're making decisions based on a thousand people versus a clinical trial with 30 or 40, which makes statistically a pretty bad sample. What would you, could you please explain the Answer Fund Program and how it will benefit patients?

Anne: Right. Well, and you teed that up perfectly in terms of the answers in the data. So what we started to observe, I say about a year ago was that, we're thrilled that, at that time there was like 40 different abstracts or publications, analyzing the compass data. But it was all questions that an individual researcher was asking, would say what, I'm interested in this target or I'm interested in predicting, you know, high risk, whatever it may be. And, and that's, that was what was published or presented. So we, we, we thought, what, these are not necessarily questions that patients would have or would have, immediate or short term benefit for patients. So we launched what we called the Answer Fund. It's basically a pot of money to answer questions using the CoMMPass data and other data sets as well, to answer questions that matter to patients. So we put out the first one is still around high risk. It's, I think as everyone in the panel would agree is still the grid, the area of greatest unmet need right now. So we put out an RFP and we'll be announcing the winners shortly for that. And that's really around coming up with figuring out a better how to validate, some kind of, whether it's biomarkers are pretty predictive signature. And then, potential treatment options for a high risk or at least some subset of high risk patients. We also, last fall, and I know a number, some of you Jack included, helped us test this, through a company called Ideas Scale. We went out to all the patients in our database and on social media to say, what are your questions? What questions would you like to see answered using CoMMPass data. We had something like 200 different questions, many more interactions in terms of people liking other people's questions or commenting on them. So we're in the process of selecting a question and putting it, which probably but don't quote me, this will be around maintenance therapy and putting that out for an RFP in the first half of this year. So again, kind of stay tuned for that, but the Answer Fund really is to make sure we have money set aside to do analytics on questions that don't matter just to, you know, researchers in the lab but also to patients,

Priya: Yes. And Jack probably you can ask your question for Anne.

Jack Aiello: Sure. And, a belated happy new year. So all my questions are related to a webinar that was conducted by the MMRF, specifically Faith Davis, Drs Faith Davis and David Siegel gave it earlier this month

to, discuss what happened at ASH, but Dr Davis also talked about a trial called, referred to as My Drug. And so I had a few questions on it because it was unclear to me, she presented a slide that said it is for functional high risk patients. And so I was wondering, does functional high risk mean different than high risk, does it perhaps mean dual deletion 17 p 53 as per your comment earlier or can you, can you expand on that?

Anne: And for those of you who weren't on the webinar, it was earlier this month and highlights from ASH. And this specific slide came from a presentation that our head of research, Dr. Daniel Auclair presented at ASH. And it wasn't on My Drugs specifically, but it was on a different study. The study's not longitudinal, but it is sequencing relapsed patients. It's our molecular profiling protocol. And we've sequenced almost 400 patients from that and Daniel was presenting the data in terms of how many patients as a result of, being sequenced, got into a clinical trial, got on a targeted therapy. What was the frequency of alterations reported, and he showed this at the end, this slide of the end and talking about my drug, because it's our way of, kind of, the final step in terms of precision medicine. We're generating data through CoMMPass and other initiatives like that, we're dedicated to the analytics through partnerships with folks like TNS driving analytics through the Answer Fund and then, but to really matter to patients, we need to drive into the clinic. And because of some of the mutations that we see, either through our original genomics initiative or through CoMMPass may only be seen in five, 10, 15 percent of patients, the best way, the most efficient way or probably the only way to do this in a disease called multiple myeloma is through a master protocol or platform trial. And this is where we would screen patients.

And Jack, I promise I will get to your question, just to give everyone the background, we would screen patients, using that panel, and then if they had one of the alterations that was in one of the, six to eight arms, they'd be assigned to that arm. And if they had nothing, they would be assigned to a control arm. And again, all of these, arms with the trial, it's one single trial. So we're not opening eight separate trials and trying to come up with, it would take many, many different sites and it would take a long time and costs a lot of money. So doing, I spy, for those of you who may have heard of this, is that kind of study, you have one protocol, but then you have different, more than two arms, which is obviously one or two ours, which is standard for phase one, two, three trials. So to answer your question about functional high risks, if it's true, it has nothing to do with genomics or anything else. It's have you relapsed after initial therapy within two years. That's what we're calling functional high risk and it goes back to a lack of, consistency or validation or predictive ability to say who truly is high risk. So we're going solely on the dual failure initial therapy within and are progressing your initial therapy within two years. And then the arms, the current arms of the trial mostly not, not entirely, are associated with higher risk, by our targets, it may indicate higher-risk disease.

Jack: So it's for relapse or refractory patients who have relapsed within two years of initial treatment?

Anne: Correct.

Jack: And is it taking patients from CoMMPass or just completely open to those patients that qualified for what you just indicated?

Anne: Oh it is completely open to those patients who qualify. We're looking at opening it at hopefully all 25 of our MMRC, our clinical research network sites, potentially others as well. And we'll also, whether it's CoMMPass or probably more the molecular profiling protocol because FDA with these types of studies would like patients to be screened using one assay because again, there's, there's quite a bit, there can be some inconsistency. So if, for example, you were profiled, six months earlier we could, we could alert your doctor, hey, that patient has this alteration, he or she may be eligible for this trial. So you may not need to get another bone marrow to, be tapped for this or at least told about it.

Jack: So I know you're aware that a couple years ago, a few years ago, NCI opened up something called the Match Trial, which looks at different cancers, but it again looks at mutations associated with those cancers and if you have one of those mutations, it gives you a particular drug that's effective against it at recently opened up for myeloma. So is this similar to that except for the fact that it will be specifically for myeloma and handle more patients?

Anne: So it's similar, you bring up a good point there. There are different ways to set these things up. You can do it by disease and then the arms of my target or you can do it like NCI did. It's really targeted and the disease, then the disease falls under the target. I haven't checked, I will do so after the call. I don't believe any of the arms overlap, I think in the match trial, but I'll, I will at least with you, Jack, separately confirmed this, that they have different alterations because these, most of the ones here, not RAF and RAS, but some of the others like FGFR3, it is seen in a couple of others like bladder cancer, but it's mostly a myeloma alteration versus obviously NCI was looking at alterations that are common across many different cancers. So like a, B-RAF, which I believe is part of the match study and we don't have that.

Jack: And by the way, just for the audience sake, you're calling it alteration, I'm calling it mutation, but we're talking the same thing, right?

Anne: Yes, yes, yes. I've been trained by my side. I haven't, the scientists say alteration, but yeah, same thing. So I guess mutation suggests something bad and perhaps an alteration made be good, maybe something that confers a better prognosis.

Jack: Ok.. I'll go by that, on the, on the chart. I'm trying to understand also if it said, for example, let's look at the looking at the chart which says if you have T 11, 14, it says the treatment would be a PCLI plus a backbone regimen. And I assume you're talking about like something like the Venetoclax, correct? And I wonder what the backbone regimen is and as the backbone regimen the same for all of these different arms.

Anne: Yep. So yes, the backbone regimen is, it's our Ninlaro-Pom-Dex. So it's all oral and, at least in the case of Pom, you know, maybe a little bit, I guess there's an assumption too that perhaps you've failed Revlimid already. So going to to Pom and then the convenience of all oral. Oh, I was just going to say for the, so we're approximating 40 to 50 percent will not have one of these actual actionable alterations or mutations. So they would go into, they would be the quote unquote control, but it's not really, I wouldn't say it's so much a control as we're looking at two arms for that one and one of them would be, a novel immunotherapy, like a BCMA, a antibody or by, and then the other one, TBD.

Jack: Got it. And when to expect this trial to start opening up?

Anne: Q3 of this year

Jack: And I always appreciate talking with you and your very clear answers and I'll turn it either back to Gary or just forward it to Cindy.

Cynthia: Hi Anne, how are you doing?

Anne: I am good. How are you doing, Cindy?

Cynthia: I am good thank you. So what I would like to learn a little bit more about is I see that, you know, the MMRF founder Kathy Giusti is part of this Kraft precision medicine accelerator project. Can you tell us a little bit about what that project is?

Anne: Sure. So its a program of the Harvard business school, Robert Kraft, a very successful businessman for those of you who know, who the owner of the patriots is. So depending on where you live, you may feel one way or another about him, but truly a tremendous philanthropist as well. So, his wife, I'm a few years ago, was diagnosed with ovarian cancer late stage. She and obviously they live and they lived up in Boston, I had heard, was able to have her tumor sequenced and she did have an actionable alteration mutation. But sadly she passed away before being able to get into the trial. So he feels very passionately about cancer and making a difference in cancer, but also about the promise of precision medicine. But interestingly, when he decided to make a donation of $20,000,000, he made it to the business school and not to the medical school or to the Broad institute or the many, many other amazing research programs up in Boston. So once, you know, Harvard business school, got the funding, the dean reached out to Kathy because, he knew that,

she'd been very much focused on precision medicine and one cancer to say, would you serve as co-chair with Richard Hamermesh who's a professor of emeritus up at the business school.

So Kathy has been co-chair for a couple almost coming up on a couple of years there. It's, she splits her time. Although splitting her time means she's pretty much a 100% MMRF, a 100% up there as well. And she structure she and Richard structure the program, or really the goal is to bring best practices of precision medicine to all cancers. And you know, similar to what we were talking about in terms of the MMRF sharing data, it's really about sharing knowledge, sharing best practices. There are four different work streams, one focused on data, one focused on direct to patient efforts, one focused on innovative trials and the initial focus is platform trials like My Drug and one is on new funding streams like Vent, you know, alternative funding stream, non philanthropy like venture. And so within those four areas, there's a leader, there are leaders. The leader on clinical trials, for example, is Dixie Esseltine. So for those of you who have been around a while, she was, she helped bring, Velcade to market and it was at millennium indicative for a very long time. And each of them has a number of different non-profits and we meet and share best practices, but also, both within ourselves but also with the goal of publishing. So Kathy and Richard have already published a number of articles within Harvard Business Review. They're launching an executive ed course in the fall. I'd say for me, I sit on the direct to patient group with four other cancers and it's been tremendous on the data side. And one of the first projects of the, the accelerator was to put together a full landscape of all of the cancer data sets, for profit, not for profit, public domain, not public domain and the Harvard business school library keeps that maintained. And that's available to anyone who wants to understand what the data landscape is. And you know, our CoMMPass study was, it was, circles four quadrants and circle showing how the data in CoMMPass really stood out. But on a direct-to-patient side, there are some other groups who are doing amazing work and have successfully done things that the MMRF hasn't.

So the pancreatic cancer network. Pan-Can is one and you know, it's one of those things where the MMRF is sharing knowledge and so it's, going beyond the myeloma field, but we're also taking learnings back as well. So there's things that I personally have learned that have really helped, I think made the MMRF stronger in terms of some of our patient engagement and outreach strategies and then even on the trial side, a couple of the trials like I spy and others had been underway that we can learn from and optimized and allow us to optimize My Drug before we launch it. So there's tremendous, tremendous synergy and again, we're certainly having Cathy up there sharing a lot of what we've learned, but we're taking a lot back as well to the foundation and the community.

Cynthia: I agree it's wonderful. Even like when patient advocates across cancer sites come together, we learn from each other and help each other out. So the other question maybe to go a little bit about is I think the MMRF is launching or has launched the molecular profile on this, can you tell us about that? Is it recruiting patients? And explain a little bit more about that.

Anne: So that's what I was referring to, when I started to answer Jack's question. So, it's a way for patients who are not enrolled in CoMMPass. It's opened to the technically the protocols open to all patients, but we are focusing on relapsed patients, in terms of those patients, having much more need for options and newly diagnosed patients. So if you're a relapse patient and you're looking to have your tumor sequenced, I believe it's open at all 25 MMRC sites. If not, it's, it's at least 20 of them. We launched an RFP a couple of years ago, university of Michigan – one, it's a myeloma specific panel within 7 to 10 days, your doctor, requires a bone marrow biopsy, but, your doctor will get the results within seven to 10 days and it's a very clear, simple report to say, ok, you have this mutation, here's a list of trials for you or here's some off-label therapies. So what happens in those 7 to 10 days is the sample sequence and then a tumor board of doctors who looks at it to help provide that report. As I mentioned earlier from the data that Daniel presented a lot of about 60, 65 % of patients have had an alteration and the vast majority of those have been, or a significant number have either been put on a trial specific to that for that alteration or off-label therapy. So when we talk about, generating data, we also pull these data sets together because CoMMPass, we have limited data on relapsed patients. But here, we already have about 400 and in a few cases we have multiple samples on the same patient. So we pulled together our own datasets in addition to, looking for others that may be willing to share data.

Cynthia: So for any relapse patient that's on the call, if they're not going currently to one of your sites today, make a consultation for those sites in that, …?

Anne: Absolutely, yeah, to get in touch with our patient support center, which is 866-603-6628 and that's probably the easiest way to do it or if you're more assertive, I want to do it yourself, just look up on our site, one of the 25 different centers, and it's called the, you'd get a consult. The molecular profiling protocol. And we started with 500 slots we've seen was about 400, but we're where we are looking at expanding because there's been no great demand and certainly really good feedback from the doctors and the patients.

Cynthia: That's good to know. Speaking of these biopsies that you have to have any part of this NCI initiated, what is the MMRF doing along the lines of liquid biopsies and why are they important? Why, why are we hearing all this information about liquid biopsies now.

Anne: So this is an area that there's a lot of discussion at the MMRF and certainly, you mentioned it and it's been in the headlines I think in a number of these meetings. So what we've done, we have supported, through funding, some of these efforts, specifically Suzanne Trudeau up and Princess Margaret. But we're, we're doing putting this into practice is for patients who are on CoMMPass and who relapsed. We'll be collecting both bone marrow and, also we will be sequencing the blood but also the bone marrow but also the blood. So that's exciting and hopefully the bone marrow piece can go away. The challenge right now is these blood liquid biopsies are not clear grade yet. There's at least we haven't found one. If anyone on the call knows, let us know. But there's no clear grade one available, which means the results can't go back to your doctor. So with our molecular profiling protocol, because it is clinical grade doctors can make clinical decisions based on the results of the, the panel, there's no clear grade liquid biopsy yet. So I will tell you though, as a 2018 priority, we are very much focused on identifying the right partner, but how do we make this, make it clear grade, so that it could potentially in the not so distant future replace bone marrow in terms of patients being monitored or receiving the same information in terms of genomics, immune, what have you, MRD simply from a blood sample as opposed to needing bone marrow.

Cynthia: That would be great and Gary please ask your questions.

Matt: So for the CoMMPass study, did you include individuals with smoldering myeloma and if not, why not? And if so, what are some of the findings in terms of treating or not treating and things like that?

Anne: So CoMMPass did not include smoldering patients. And, the reason was was because part of the eligibility criteria was requiring immediate treatment. So obviously, you know, right now smoldering, myeloma patients generally aren't treated, and require treatment with an image and oral proteasome inhibitor. So I've been thinking about what I, what I say this on the call, but because there's been a couple of different places, but I think now is a good time, keeping with the theme of data generation and building out a data bank to answer, to be able to give every patient exactly what he or she needs in terms of the right treatment, the right combination, the right sequence, and also answer all the questions that patients in the community have. We are, we will be this year, in the first half, the first half of this year, announcing an effort to build upon these datasets, CoMMPass obviously being the largest.

And it will, that, that effort will include all patients including smoldering, So if you are smoldering or if you're, 15 years out, having been through many different lines of therapy, you would be eligible to become part of this next wave of data collection. And there would also, back to Cindy's question, be a part of that would also be a liquid biopsy. So collecting data using blood samples versus bone marrow. So, I can't say a lot more about it yet, but certainly I'll keep everyone closely posted as we get closer to being able to announce this, but we're really excited about it. We hadn't thought a couple of years ago that, that type of effort may be necessary, but in terms of trying to find enough data to, again, to answer these questions, it's been harder than we thought and technology is allowing us to launch a CoMMPass like study for much less than $40,000,000. So we're really excited about that.

Matt: Ok and I'm curious, looking at some of the stats in the CoMMPass study, how do you reach out to

people and how do you get people to join? And I think the thing for me that jumped out is the percentage of African Americans in the study is pretty low and I'm wondering why that is or does that represent something bigger?

Anne: So it's, it's funny you say that because why one reason why we're proud of CoMMPass, thank you for bringing this up because I did mean say to earlier, it really does generally represent the full face of multiple myeloma. So when you look at clinical trials, they're often biased toward, a little bit younger patients, a little bit healthier patients, African Americans tend to be underrepresented actually. The proportion of myeloma patients who have, who are African American is almost 20 %. So the 16 % is actually really good. It's only a little bit smaller than the full representation. So we're, we were pretty proud of that. It's not that. So it sounds low, but it actually represents the proportion within the greater community and when you look at, things like age, we had patients enroll who were, I wish I had these stats in front of me, I don't, who I think were like in their early 20s to early mid 20s and then all the way up until their late 80s. So again, particularly those elderly patients may not be those in clinical trials. But we have again, a study that does represent, a pretty good snapshot of what myeloma looks like in the US. Another point that you didn't ask, but it relates to the very first question that Gary asked in terms of what we're learning. One publication that came out late last year of looking at CoMMPass data in African Americans in the CoMMPass data interestingly found that a couple of, couple of things. One, there was a lower incidence of high risk disease. So, for African American patients they were less likely to have some of these traditional high risk features. And then the second piece, which is, what we've seen too is that when treated the same, when receiving the same treatments, they do, there is no difference in terms of outcome based on, race, race, or ethnicity. So when you see particularly in other cancers that there are those disparities, at least in myeloma, it suggests that, given those two pieces of data to suggest that it's just getting inferior care. So as long as, patients get the same level of care they do as well or better.

Matt: Ok, thanks. And then lastly, you touched on this in your opening about findings about transplant vs non-transplant. I guess is there much you can say about who transplants do benefit and who they don't? Or is there not much you can say at this point in time?

Anne: No, we don't, I have to say, and I may even take this on as an advocate, I think that's the perfect question to answer, like through the Answer Fund and, or, we hired late last year, someone on our scientific team, a PhD, who has a genomics and like a data background on that, she alone may be able to look at the data and start to develop some hypotheses. But I do think it is important for our community to start to understand, ok, we understand, and looking at the entire population, having an early transplant is better. But when you start to drill down to specific patients sub-types, are there ones who doesn't really matter and/or are there ones who just should skip transplant altogether? Because based on their alterations, there's no way that, you know, there's, they have a low probability of getting a good, real good or durable response.

Matt: Ok, that's all I have. Thank you.

Priya: So, we can take some questions from the audience now. If you have a question for Anne please press 1 or email me at priya@trialx.com. Now we have a couple of questions already come in, so the first one is which is accelerated phase of development, the physician medicine initiative and other programs that MMRF is leading, do you predict a tentative timeline by which we can expect to see myeloma cure?

Anne: I wish I know I'd say where one topic that didn't come up earlier, and this is another program that we launched last year that we call the prevention project. And really the goal long term would be prevention, but in the short term, can we prevent progression from smoldering to active myeloma? Can we prevent progression from mgus to smoldering? That kind of thing. That program, again, it's only been up and running for the past 6 or 7 months probably is our best shot of getting to cures if we can prevent active myeloma from ever happening. I think it's still too early for if a patient is diagnosed today. But what, what we certainly, that's always, always our overarching goal. But in the meantime, can we continue, working with the entire community to extend patients lives and at the same time not having them on therapy forever or not, some have a terrible quality of life because of the side effects of therapy. So again, meaningful life

extension but also meaningful quality of life.

Priya: Thank you Anne, another question, what advancements can we expect to happen this year in high-risk myeloma management?

Anne: Certainly, the launching of our, My Drug protocol is important. We also, so kind of stay tuned for that, if that is a study that, as we talked about is for first relapse, so it will be somewhat of a narrow population, but we're also launching another platform, multi-armed trial of immunotherapy specifically. And that's kind of an interesting one because that trial was pretty much already to launch, late last year in the fall last year and that's when the data around Keytruda or Pembrolizumab, came out and FDA halted all pd 1 and pd-l1 trials of any disease or in myeloma. And in any combination, any of those agents. So it forced us to, and probably better than we hadn't launched it, forced us to rethink, you know, kind of re put that together. And so we will, we're planning to launch this year a new, another immunotherapy multi-arm trial and not will specifically be for relapsed refractory patients. So, high risk, obviously it can be defined in so many different ways. There's genomically high risk then there's, I'd say at some point, most relapsed refractory patients falling into that category simply because their likelihood of responding to treatment are responding very long, becomes lower. And as we start to see patients progress off of Darzalex or Daratumumab, those patients probably should be called high risk as well. So this trial, would be for those patients, again, not genomically high risk, but high risk in terms of, in need of, of new and better options.

Priya: Thank you Anne. And, I think we left one of Gary's questions unanswered again, you've been mentioning clinical trials for high risk patients. So, what are the other trials that MMRF feels can be the next steps to treatment and cure, that's one question, probably you could just mention some of the clinical trials that are in process or in development that a patient needs to keep track of.

Anne: Yeah. And so, through us, I think the two big ones launching or these two platform trials, and then we have a number of other trials both molecularly targeted, also, we launched last year for the first time trials and plasma cell leukemia and also patients who have amyloidosis. So those are ones that we're doing. I think, across the board the excitement around CAR T is undeniable and, and some of these other antibodies and immunotherapy approaches using the same targets like BCMA. So we are, as I mentioned in My Drug, one of the arms we're looking at would be using possibly a BCMA in the non mutated arms. And then we are, one of the other things we launched or announced last year was a $15,000,000 investment in immunotherapy, because, and this is kind of a perfect wrap up to all this discussion.

For a long time, precision medicine was genomically based. We're now seeing that, our view is that immunotherapy should be precise as well when we look at these patients who have unbelievable responses to some of these CAR Ts to the BCMA CAR T why is that? And so we launched and we committed $15,000,000 to advancing some of the most exciting immunotherapy like CAR T, but also to invest heavily in correlative studies to understand who's most likely to benefit. So there is a tremendous amount of enthusiasm still for genomics, but it's only part of the answer and may not be relevant for a lot of patients. Immunotherapy is certainly, requires a lot of investment and attention as well.

Priya: Thank you Anne And thank you so very much and keeping us abreast with all of MMRF initiatives and progress. And we're almost to the end of the talk time right now, Gary, Jack, Cindy and Matt, thank you all for your participation and the talk will be made available on the CureTalks website, curetalks.com for details of our upcoming talks. Thank you everyone.