Myeloma 2015. Year in Review with the MMRF

2015 saw a lot of action in the Myeloma world. Four new drugs were approved by the FDA increasing treatment options and allowing new combination regimens; promising immunotherapy research results will see these being used in clinical practice and 1000 myeloma patients have been enrolled for the MMRF's CoMMpass study. We are talking to Anne Quinn Young of the MMRF to understand the significance of progress in myeloma research in 2015 for the myeloma patient community as well as review MMRF research initiatives in the last year and what patients can expect in the coming new year.

Full Transcript:

Priya Menon – Good evening and welcome to CureTalks. I am Priya Menon, Scientific Media Editor of CureTalks, joining you from India; and I wish everyone a very happy new year. We begin this year with a review on myeloma research and activities in 2015 with the MMRF. This is CureTalks' 99th episode. My co-host for today's talk is myeloma survivor and editor of myelomasurvival.com, Gary Petersen; and supporting Gary on the panel are members of our myeloma panel, Pat Killingsworth, Jack Aiello, Cynthia Chmielewski, and Matt Goldman. Welcome to the first talk in 2016, everyone.

Priya Menon – It is with immense pleasure that I welcome today's featured guest, Anne Quinn Young of the MMRF, to CureTalks once again. Great to have you on CureTalks, Anne. 2015 saw a lot of action in the myeloma world. Four new drugs were approved by the FDA, increasing treatment options and allowing new combinant regimen. Promising immunotherapy research results will see these being used in the clinical practice. What does all this research progress and drug approval signify for the myeloma patient community? In the hour-long discussion, we will also be reviewing MMRF Research Initiative in the last year and what patients can expect in the coming new year. With that, its over to Gary. Gary, you are on air.

Gary Petersen – Well, thank you very much, Priya; and as always, we in the myeloma patient community and…, and those of us who are myeloma advocates certainly appreciate all you do for the myeloma patient community and also would like to thank Anne Quinn Young for all the MMRF does for the myeloma patient community. I think that the fact that we brought four new drugs to market in one year, which I am pretty…, pretty sure that's probably 20% to 30% of all cancer drugs for a cancer that represents just 1% of all patients, means that a lot of people are doing a lot of things right in order to bring these great things to the market. So, I…, I certainly do appreciate that and welcome you, Anne, to the…, to the…, to the program; and thank you and everybody, including Kathy Giusti, for all her fine work. So, with that, I am going to turn it over to you to give us a…, a rundown of what's happened at the MMRF in 2015 and what's your plans for the future?

Anne Quinn Young – Well, thank you so much, Priya and Gary. Priya, congratulations on the 99th program; and thank you so much for having us back in the show. Its always such a pleasure to be here and an honor to represent the MMRF in front of all these incredible patients. As you have just heard and…, and I am sure most of you had already known, 2015 was really a historic year for myeloma as…, as both Priya and Gary mentioned. We had four new drugs approved, including three during a whirlwind three weeks before the end of the year; and what's really even more exciting about these four drugs is that they represent two brand new processes. The first one that was approved about almost a year ago is the first HDAC inhibitor, which is panobinostat or Farydak and that is typically used later on in the disease and works very well with Velcade, but its being looked at in a lot of different combinations and stages of the disease and then the first two antibodies before the end of the year, elotuzumab or Empliciti and daratumumab or Darzalex, were again the first two antibodies ever approved for this disease and they have the ability to really transform the treatment of the disease possibly as early as, you know, first line or even in smoldering patients.

Anne Quinn Young – Some of the trials are looking at those treatments in…, in early population and then the first oral proteasome inhibitor ixazomib or Ninlaro and…, and for those of you who may be new to this, as a

reminder, the proteasome inhibitors are Velcade and Kyprolis and together with IMiDs and steroids tend to form a common backbone of therapy and as…, as…, as Gary mentioned, it really…, its somewhat surprising and for those of us who have been in the field since…, before Velcade was approved almost 13 years ago, its exciting but perhaps not so surprising because of the amazing community we have in this disease. The collaboration between doctors and researchers, companies, patients, groups, groups like our's, groups like this, its incredible; and, you know, for us as an organization, we are continuing to build on the model that we have had in place since our inception and…, and what our goal is is to accelerate new treatments and cures and in the foundational model for this is our end-to-end system in precision medicine and when I say precision medicine, you know, we are not just talking about genomics, but we mean it in the broader sense that we are trying to find the right treatment or the right combination of treatment in the right sequence for any myeloma patient.

Anne Quinn Young – To lay it out simply, we look at three different components and you can feel free to visit our website afterwards and learn a little bit more, but to suffice to say it starts with our data bank and in a heterogeneous disease like myeloma, everyone in this line, I am sure, knows that you have very different type of myeloma than, you know, the person sitting next to you in the cancer center and even within patients, there are different clones. So, its a very complicated disease. Its also changing and this…, all the time. This means we need a critical mass of high-quality genomic and…, and clinical data. The MMRF was the first to launch genomics initiative 10 years ago in the disease, long before there was a genomics initiative in any cancer, including the solid tumors by building a collaboration between the centers and genomics experts like Brodin P, myeloma was the first genome to be sequenced because of the collaboration that we put together, but we didn't stop at that 250. We realized we really needed longitudinal data, clinical match with genomics and…, and that's where the MMRF CoMMpass study was born. We now have 1,000 patients…, 1,000 myeloma patients enrolled to be followed over eight years from the point of diagnosis through each relapse, collecting all the clinical data and doing genomics sequencing on whole genome sequencing, whole exome sequencing, RNA sequencing, and I am happy to say we now have the largest genomic data that of any cancer…, any cancer. We have… There are more than 800 sequences available; and through the learning network, we feel very strongly about pushing that data out into the entire world.

Anne Quinn Young – When we put CoMMpass together, we didn't want anything slowing down the dissemination of data. We wanted to make sure it wasn't just the 90 centers that were working on the CoMMpass study that had access to it, but all the brilliant minds across the world, across disciplines as well. So, we made sure that there was no IP related to the study that any inventions went into the public domain. We have also formed partnerships, like one with GNF Healthcare to use artificial intelligence computer programmings to map the pathways much faster than could be done in a lab; and in the final step in the model, collecting and aggregating the data and making it available, analyzing, and then its driving it to the clinic because at the end of the day, that's what's most important; and through our clinical researching network, the MMRC, we continue to open 6 to 10 trials a year, focusing on novel classes like HDAC inhibitors and…, and…, and some new ones that haven't yet made it to market, targeted treatments and those are based on molecular alterations. So, if you have a specific genomic mutation, there may be a treatment for you as well as immune.

Anne Quinn Young – So, you know, when we look back at 2015, certainly, you know, what dominates, is the four drugs approved, but for us we completed enrollment of the CoMMpass study. So, we hit that 1,000-patient mark in about four years. As I said, it took 90 centers, 4 different countries, and you know, a lot of folks working together and what… what's really me…, to me personally is now I am finding that, you know, all over the place I am meeting CoMMpass patients and its…, its really inspiring to me because they understand what they are part of. They understand the values of the field and to the value to them specifically and…, and that is very different than the world was five years ago when I think genomics was a much more overwhelming topic for patients.

Anne Quinn Young – Recently, at…, at ASH in December, the American Society of Hematology meeting, we presented the first real clinical findings from CoMMpass and…, and CoMMpass is starting to answer some really important questions to patients, you know, one being is it really more beneficial to be on a triplet versus

a doublet. Now, the vast majority of academic centers are treating patients upfront with a triplet versus a doublet, but does it matter and indeed, we did find that there is a significant difference in terms of time to progression for patients who were treated with a triplet versus a doublet. We are also starting to see that across a lot of different variables, having a stem cell transplant earlier is advantageous and…, and…, and you know, we need to delve down to try to figure out are there certain groups of patients where that may or may not…, that may not be the case, but having some of the larger questions that we have some additional light being shed on them is incredibly important and allows patients to have a better idea of how to proceed on their treatment course; and on the clinical trial front, we opened six different trials and what was particularly exciting about these trials were the first two for smoldering myeloma. In the past, we had focused on upfront treatments as well as relapsed refractory and last year began a trial with daratumumab or Darzalex as well as one with elotuzumab or Empliciti plus Rev-dex. We also opened the first targeted trial for a patient population with a specific alteration and that an MDF2 inhibitor from Roche in combination with the oral proteasome inhibitor Ninlaro for deletion of 17p patients and in the third trial that was particularly interesting was the first PD-L1 inhibitor to be studied in…, in myeloma and that was open across MMRC centers as well and then finally we launched late in the year a screening program with University of Michigan where we are able to sequence relapse patients who are seen at MMRC centers and…, and there is potential to expand it beyond MMRC centers as well, to sequence them, and then to match them to trials like the MDM2 inhibitor and Ninlaro and others that we are planning to open this year that focus on a specific patient population.

Anne Quinn Young – So, switching gears a little bit into 2016, you know, when we look at our main focus and its only three weeks into the year, but its pretty clear that one of…, one of…, one key area of focus has to be to figure out how these…, all of these treatments…, now we have this, you know, almost embarrassment of riches of 10 drugs available, you know, 6 of which are probably going to be seen at multiple times in…, in a patient's treatment course, you know, what is the best way to combine these…, these drugs, to sequence them, to dose them, to combine them with investigational agents and really start to answer some of those questions from investigator initiating trials through the MMRC and also starting to look at CoMMpass and other data sets.

Anne Quinn Young – A second main focus for us is really continuing to, you know, advance the precision medicine model and really push towards the clinic. So, we opened at the end of last year our first targeted trial and…, and we plan to open a couple more this year and then look at broader protocols where we can screen many different patients at once and…, and put them into the right arm for them and then finally, and you'll hear more about this later in the year. Late last year we also completed a quantitative patient survey on the myeloma patient journey and so we will be looking at all of our educational program offerings and perhaps listing the help of some of you on the line as well to make sure that we really are meeting the needs of patients at every point. So, you know, really and closing before we move to the Q&A, you know, the progress really has been absolutely, absolutely stunning and it gives all of us such hope and inspiration when we see patients living to see milestones and celebrations that they thought perhaps they would never see. On the flip side, you know, we are not there yet. You know, the disease is still largely incurable and…, and around here driven by Kathy, our founder, you know, we…, we firmly believe its not the time to become complacent, that we still see patients relapsing and…, and still see this really complicated, determined disease becoming more difficult to treat as time goes on. So, we are inspired by the progress. We are incredibly hopeful this disease looks very different than it did even five years ago, but I can assure everyone on the phone that we are not taking our foot off the accelerator. We are pushing to…, to get more extensive remission made possible by treatments that have fewer side effects for every single patient. So, I'll stop there. Again, thank you so much for this opportunity and I look forward to the Q&A.

Gary Petersen – All right. Well, thank you, Anne. That was excellent. We really do appreciate it and we do appreciate all your efforts, you know. I.., I look at the National Cancer Institute and they provide about 54 million…, 45 million each year for research for multiple myeloma and I think you guys are already in the 275 range that you've…

Anne Quinn Young – Yeah. Over 300 over time… Yes… Yeah… Yeah.

Gary Petersen – I am always behind people like you. You guys always are ahead of me on that, but…, but the thing that…, and not only that, it is a focused and…, and…, and a business model that…, that is used and I think that's one of the reasons that we have had so much success and…, and…, and again I want to thank you, I want to thank Kathy, I want to thank everybody for this and…, and also the ASH study, which I think, you know, there's so much data out there but nobody captures it. This is one of very first attempts at doing that and I think its a gold line and…, and I really thank you for your initiative there, but at ASH, I noticed that most immunotherapy, you know, which is not a drug, but its really your CAR-T cells, MILs, and dendritic cells, you know, rose like a phoenix out of the ASH. It just wasn't really talked about in the prior year and it came from nowhere to it seemed like everybody was…, was an immunotherapist, you know, its…, that that was the big talk and it went from nowhere to top billing. So, what is the MMRF doing in this very exciting area of treatment? We have heard of all these dramatic…, dramatic results from some of the CAR-T cell and MIL and dendritic cell trials that are…, are out there, but, you know, I was wondering what…, what…., what MMRF is going to do in that area as well. It seems like the next new horizon.

Anne Quinn Young – Yeah, it…. Well, and we agree. I mean there is so much potential in…, in immune therapy and I think being able to take a lot of these different approaches and combine them is really going to be the key in terms of long remission and when…, you know, when we think about immune therapy, we largely look at three different buckets – the antibodies, this field of engineered T cells, and then vaccines and, you know, funnily enough, when Kathy started the MMRF back in 1998 and even when I started in…, in 2002, a majority of…, of our research funding was supporting researchers in the area of vaccines and, you know, a lot of that didn't really come to fruition, but perhaps it was a little bit ahead of its time and more recently, you know, particularly with the two antibodies that were FDA approved last year, we have been doing a lot of different studies within the MMRC, looking at these antibodies as I mentioned earlier in different patient populations, smoldering, upfront, relapsed refractory, and in different combinations.

Anne Quinn Young – You know, I mentioned the PD-L1 inhibitor trial really, really exciting and rolling like gangbusters through the MMRC and what that does is its a checkpoint inhibitor, so instead of these other antibodies which target primarily receptors on the…, the surface of the myeloma cells, they do, you know, have an impact on the immune system as well, but they are really targeting the myeloma cells. What these checkpoint inhibitors do and, you know, have completely transformed diseases like melanoma, they allow a patient's immune system to recognize the…, the tumor cells and…, and really fight it off. So, instead of the myeloma cell evading your immune system, the checkpoint inhibitors, you know, can serve to kind of wake it up and…, and…, and help your own immune system, you know, fight it off. So, really exciting and then you mentioned the area of…, of CAR-T and certainly first at ASCO when, you know, the…, the first results from the UPenn study represented and the one patient who still to this day at 18 months later, a patient who had never had even a, you know, any kind of remission to anything, including her first transplant to be in a, you know, complete remission, absolutely no evidence of myeloma is…, is amazing, you know, but again we are looking at small patient sizes. The BCMA…, the very early BCMA work that was presented at ASH again, you know, is a lead breaking session. Tons of, you know, potential and excitement just really, really early days and not at all ready for, you know, prime time in these…, these larger trials. So, you know, what…, what I can say and…, and perhaps we can, you know, talk again later in the year, we are in the process of…, of putting…, building some collaborations really predominantly in the area of the engineered T cells but also vaccines and…, and expanding some of the work in the antibody area, particularly with the checkpoint inhibitors.

Gary Petersen – Okay and…, and thank you so much for that. One of the things that I…, I…, the whole model that we have currently, you know, which is, you know, you…, you and your…, your folks are looking at drugs, you know, and doing the initial research and then handing those off and…, and ultimately its a drug company that spends, you know, the 2 to 2.5 billion dollars for each new drug that goes to market, at least that's what I have been seeing and…, and how do we fund things like CAR-T cells and MILs, which don't necessarily fit into a drug company's business plan. You know, there is potentially no billions for this development and as a result, you know, the model has to change in some way or there just won't be any funding for these things. Its kind of like a stem cell transplant, you know its a hospital that, you know, benefits from the…, from the money that a patient pays for stem cell transplant. Its not a drug company, so, you know, how you get the billions to support CAR-T cells, MILs, and dendritic cells are research and that's one of the reasons maybe it

hasn't come to fruition, very important because there is just no funding for it.

Anne Quinn Young – Yeah. Well, there…, you know, there is, I think based on some of the leukemia results from the trials at UPenn, you know, certainly there are some companies including Novartis who is involved in…, in…, in this area and then some others that, you know, financially look like they are doing pretty well like Kite or Juno, you know, forming collaborations with bigger companies as well. So, I…, I do think that there…, there does seem to be, again based on the interest of some of these companies into coming into the area that there will be interest. I think the key will really prove to…, to be, you know, figuring out the right patient population because they will be very…, it is… It will be very, very expensive to…, you know, the manufacturing, so I…, I think for companies to feel very comfortable, you know, back to precision medicine, who are the patients that are most likely to…, to respond and, you know, figuring out the right target because these…, these engineered T cells, you know, you can target different receptors and.., and CD19 which has been…, which is highly expressive of leukemia, its not expressed in myeloma. So, is that the right target for the BCMA?

So, there's a lot of work to be done in terms of, I think for finding this for multiple myeloma and then the other piece on the funding side, if…, if that does become a challenge, you know, we as an organization have supported for…, for many years now, you know, supported biotech companies with what we call the Biotech Investment Award and its really to get them over the critical hump of, you know, some of the preclinical work, even scale up in manufacturing and then into manufacturing and then into early clinical trials. So, that's the program that, you know, we don't have any new investments planned right now, but its something where we are always, you know, looking at, okay, what are some, you know, really exciting new areas for treatment and, you know, if there is a funding issue, can we, you know, potentially partner with some, you know, investor…, investors, if you will, and put some venture money toward this to make sure that these…, these approaches do have the funding they need.

Gary Petersen – I think there's some billionaire who sees the need for this and he has put some consortium together I…, I had read recently, for cancer, immunotherapy and…, and maybe that's…, maybe its…, its a whole new funding source or something like that or maybe…, maybe even the work that Vice President Biden will be doing as a new…, new initiative of the Moon Shot, but with that, I want to turn it over to Jack Aiello. Jack, you online?

Jack Aiello – Hi, Anne! Happy new year!

Gary Petersen – Happy new year!

Anne Quinn Young – Hi, Jack! Happy new year!

Jack Aiello – I think the MMRF was founded either in '97 or '98 if memory serves me right and we've known each other pretty much that whole time. So, I wish all of you at the MMRF and you as well a happy new year. I think as patients we think of the International Myeloma Foundation, the IMF, as a very patient-centric organization, whereas the MMRF is very research centric and both really benefit the patients, but just as I know the IMF has some significant research programs, I know the MMRF also offers…, offers some opportunities for patient education and you talked about the…, you mentioned the patient journey as maybe you can describe those areas of patient education that the MMRF has?

Anne Quinn Young – Sure. No, thank you, and…, and Jack, its such a…, even if its with many, many other people listening, it really is such a pleasure to hear your voice and, yeah, I think I have…, I have known you for the entire time I have been here and we appreciate all the…, the many years of…, of support. So, you know, we do…, we have a lot of…, of programs and, you know, I can kind of give you brochures of…, of again how the patient journey may impact us, but yeah, we do have a comprehensive website, you know, mymmrf.org. You can go there directly and…, and find out, you know, everything you need to know in terms of, you know, from diagnosis to treatment. You know we do have print brochures. We were always very conscious of helping patients understand all of the different options because this is a disease where we all

know that at least in the later stages combinations are important and…, and really don't kind of single out one treatment or class versus another. We are also, as you know, particularly focused on the research side and on what's coming down the pipe for treatment. We do webcast following major medical meetings and…, and those tend to get thousands of folks listening to it. Its us together with, you know, some of the…, some of our partners who just presented the data at the meetings and then we have…, have…, have the patient symposia and then the two…, two other major areas of focus are patient support center and…, and that has…, that's a little bit different than some of the others in that, you know, you can call up and…, and the myeloma trained nurses will answer any questions, but its really focused on clinical trials matching and really making it as easy as possible for someone who may be a candidate for clinical trial but has absolutely no idea, you know, how to search for clinical trials or how to get in touch with the center and…, and…, and making that as seamless and as easy as possible and then the final piece being our community gateway which really was designed as part of our overall precision medicine initiative. Yeah, it really was once we start these trials in…, in specific patient populations, whether its deletion 17p or translocation 4;14, whatever it may be, that we start to bill the critical mass of patients who then, you know, we can let them know about these trials and…, and, you know, hopefully facilitate enrollment. You know we have more than 3,000 patients on there. Many of them are highly engaged, but we will be together with, you know, the work that we are doing in terms of emulating the…, the results of the patient journey, probably doing some pretty significant changes to the community gateway to make sure that its really meeting the needs of the patients but also advancing precision medicine.

Jack Aiello – And then my second question requires you to get your crystal ball out. Its referring to minimum residual disease, MRD, and where it stands. I have been hearing about an MRD now for three to four years and yet as a patient who thinks its a procedure to get a more accurate reading of their myeloma, which it is, asks for that…, asks for MRD testing, they really have a difficult time getting this. They don't know whether MRD is defined as next-generation flow or next-generation sequencing. Should it be done with or without diagnostic scans? So, I know you have that great crystal ball and you need to tell us when the patient can…, will typically be able to ask and receive an MRD test?

Anne Quinn Young – That's a… I'll talk a little bit around it. I just… I want to make sure, you know, all on the phone really understand minimal residual disease. You know the name is…, is fairly self-explanatory, but it really is, you know, the deepest possible look to make sure that there is absolutely no myeloma lurking anywhere and why this is really important. I mean its important for a couple of reasons, but from a practical stance, you know, now that we have all of these amazing treatments and…, and patients are particularly in the front line setting, you know, they aren't relapsing for a long time. You know we need to make sure we are coming up with some new markers to be able to predict, you know, which patients may or may not need to be on maintenance therapy. For example, if you have…, if you have no MRD, do you need to be on maintenance until progression, particularly if you don't have any other high-risk features and then in terms of companies being attracted to the field, its important to be able to not have these trials go on for ever and ever, if patients…, and become very expensive and…, and, you know, take a lot of resources, are there ways to…, to have survey employed like MRD where you are…, you are potentially seeing signs of when a patient can relapse faster.

So, you know, we really are agnostic in terms of, you know, which technology, whether its next-generation sequencing or flow is superior. As part of the CoMMpass study, we are working with Antonio Colombo in Italy and a number of Italian sites to incorporate a comparison of flow versus Next-Gen sequencing and again all that data comes back into the…, the CoMMpass study and there are a number of other studies, larger studies incorporating measurement of MRD. Within our clinical research network, we are looking at studies again that incorporate MRD as an endpoint, particularly those that are looking at patients earlier in the disease course and then finally, you know, when I mentioned, you know, looking at some of these master protocol concepts where instead of having, you know, eight different protocols, we would have a master, one master protocol where patients would be screened and then depending on whether or not they had a specific alteration, they would be put into an…, an arm of the trial or put into standard of care plus experimental treatment. We…, that trial would absolutely have MRD endpoint. We have met with FDA on this. We've met…, participated in meetings with Sloan Kettering that's doing a lot of work in the field, so, you know, I would

defer to our scientist, but I…, the field is moving and there's a lot of…, there really is a lot of momentum behind this and really validating it as an endpoint and then once its clear, is there the best way to…, to measure this working with, you know, there is one predominant company in Next-Gen sequencing, you know that's something we would be… If that proved to be the best way to measure MRD, we would be fully behind, how do you bring this to mainstream practice. How do you get reimbursement done? Obviously, there's a whole host of issues, but it is a…, it is a focus of our's and…, and incorporating it into trials.

Jack Aiello – Thanks, Anne. Oh, its a pleasure talking with you.

Anne Quinn Young – Thanks, Jack.

Gary Petersen – Thanks, Jack. Cynthia Chmielewski, are you there?

Cynthia Chmielewski – I am. Can you hear me?

Gary Petersen – Are you feeling okay?

Cynthia Chmielewski – I am doing fine.

Gary Petersen – Yeah, I asked that because this is the very first time you have only had one question.

Cynthia Chmielewski – Well, I will start with a few other questions as we are talking about, but… Hi, Anne! How are you doing?

Gary Petersen – Okay.

Anne Quinn Young Hi, Cindy!

Cynthia Chmielewski – My question, talking about the data that you have been, I guess, speaking out throughout our conversation today, this topic of big data. I remember having a couple conversations with you a few years ago about how the MMRF is using this big data and I know the MMRF has this data bank that I have been talking about. Can you just explain what big data is and how this big data can be helping us to accelerate cure and how this all relates to the MMGI CoMMpass study, the gateways, and the patient registry that I feel that you are beginning to develop. That's why there is only one question. Its a big question.

Gary Petersen – Its a big question!

Anne Quinn Young – I know. Its…, it is big and I…, I covered a little bit of this earlier, but it does, you know, bear repeating because its complicated. I mean, one… I was having a conversation with someone recently…., who was recently diagnosed, a patient and, you know, he was…, he basically said, you know, its a fascinating disease if…, if someone else had it, you know. (Laughter) It…, it really… It is really fascinating in terms of, you know, again it not only differs between patients, but within a single patient, you have multiple clones. So, the…, the first one you mentioned, the genomics initiative, again that was an initial partnership where MMRC centers at the time collected patient's tissues. So, when you were having a, you know, getting a bone marrow pull, you got an extra pull for the tissue bank and then that led to the…, the first sequencing of the myeloma genome. We ended up with 250 samples and, you know, one…, one finding that is…, is very relevant today and, you know, we feel gratified by, you know, this undertaking was a mutation and a gene called BRAF and its common in…, in melanoma but had never been seen before in myeloma, is now present in about 5% to 8% of myeloma patients and, you know, you…, if you are sequenced and have that mutation, you can be put on either, you know, a BRAF inhibitor or now more commonly a BRAF/MEK inhibitor and…, and potentially go into a complete response.

Anne Quinn Young – That's one of the trials that will be opening through the MMRC later this year and…,

and that was only possible because we had a deeper look at the disease until…, until then, you know, it was conventional cytogenetics and FISH which is still done, you know, predominantly even at community centers or gene expression profiling. So, bringing sequencing, the sequencing technologies to myeloma, again, you know, brought forward something that had never been seen before and so we…, we built on that with CoMMpass and, you know, the interesting thing about CoMMpass is its now a 1,000 patients and its longitudinal. So, that means, there will be literally thousands of samples that are analyzed, but the…, the truth is with the heterogeneity of the disease, you know, we are looking at combining that with other data sets to get, you know, the…, the most robust look at…, at this disease as possible and so, the idea behind the CoMMpass and then building out the researcher gateway where all the data is publicly available was that other centers would share their data as well as we continue to build our CoMMpass and follow patients longitudinally. So, you know, that…, that's really our goal and our hope and we are still…, we are still looking for that first set to say, look, we'll…, we'll give you…, we'll contribute the data and then, you know, the next step that you mentioned is building out a registry and, you know, that…, that is the next logical step in terms of, you know, expanding beyond this 1,000 patients, how do we start to collect data on thousands of patients. So, its something that, you know, the 1,000…, the CoMMpass, you know, we wanted to do it right now. It took some planning and we want to make sure that when we do launch a registry, that again it…, it really is meeting all the needs of…, of the field and…, and really helping to advance new treatments and cures for patients.

Cynthia Chmielewski – Thank you so much. Will the registry include when you go there, patients that are relapsed refractory? I know the CoMMpass study had just been newly diagnosed?

Anne Quinn Young – Yeah, the…, you know, again, its a little… Because we…, there is no protocol yet for a registry, you know I can say though that we are…, we would be looking to be as inclusive as possible in figuring out ways to make sure that its available to, you know, the patients can enroll and contribute their data whether they may be relapsed refractory, whether they are at a center that's not part of the clinical research network, which either tend to be large academic centers or centers that are predominantly community centers but in…, in urban areas. So, that's why its…, its quite a daunting task, but we're, you know, we're really looking at the…, the landscaping and seeing that there is a lot, you know, I think what…, what we really see is that there are lot of these silos and these…, these desperate efforts and…, and… and we want to bring it all together and certainly not duplicate any efforts and…, and maybe there are ways to build upon existing efforts without, you know, starting from scratch.

Cynthia Chmielewski – That sounds like a good plan. Thanks so much.

Anne Quinn Young – Thank you.

Gary Petersen – Thank you, Cindy. Matt Goldman, are you online?

Matt Goldman – Yes, I am. Hey, Gary! Hey, everybody! I just have one question. Maybe this is just my perception, but it feels like that age of myeloma patients seems to be trending younger. I don't know. It just sort of seems like that, but I wondered if…, if the MMRF initiative data gathering if you are…, you are doing any research from the patient demographic profile to see if there is any common theme or maybe look at actual causes of myeloma, if there are environmental factors that maybe would jump out from all those data. Any of that happened?

Anne Quinn Young – Of course, there's a few different questions rolled into your one question.

Matt Goldman – Yeah.

Anne Quinn Young – So, the first one, in terms of the…, the age of diagnosis, to my knowledge, the median age is still, you know, somewhere around age 70, but I…, I think as we all know it can…, sometimes it can take, you know, a while for data sources to catch up because I have certainly seen, it seems like there are younger patients. We are…, through CoMMpass, one thing I didn't mention that that we are quite proud of is

its really a snapshot of the disease, at least in…, in the US, in that, you know, we have, I think patients from age 19 to 91 enrolled and they are at about the…, the proportion that you would see naturally occur, you know, that are naturally occurring across all diagnoses. We also have, you know, proportionate representation from different ethnic groups and so you hear African-Americans being under represented in…, in clinical trials. Well, we through CoMMpass, there is proportional representation.

Anne Quinn Young – So, we really are, you know, looking at this as a snapshot of…, of what the disease looks like across many, many different variables and so I think that will start to perhaps shed some light too on whether myeloma that's…, that's diagnosed younger versus older is at a different kind of disease. You know I do think that…, that what I have seen at least in my 13 years is that diagnoses are happening earlier. Without a doubt, there are far more smoldering patients and…, and patients are being diagnosed following routine blood work for physicals, insurance versus these very, very sick stage 3 patients that seemed to be the…, seemed to be very common, you know, many years ago and…, and its important because hopefully there is that window to better control the disease at an earlier and perhaps, you know, if…, if one of these antibodies work to prevent the disease in smoldering, maybe a smoldering patient never develops full-blow myeloma. In terms of causes, you know, we are still because of the…, the nature of the disease and…, and the fact that again the vast majority of patients still relapse, we are…, we are very much focused on treatments right now, although as I mentioned earlier, we are…, we had never looked at smoldering before because the…, the…, the need really was predominantly in relapsed refractory and making sure that when patients, you know, ran out of options, there were other things in the pipeline for them. Now that we have this robust portfolio of approved drugs and still ones coming down the…, the pike or drugs approved for other…, in other diseases, we are looking earlier in terms of newly diagnosed and smoldering and then there are some studies now looking at can we…, are there hereditary predictors? I don't know how many of you saw the Wall Street Journal article toward the end of last year featuring Kathy and her family, which, they are significant not just for myeloma, significant cancer, and…, and opted to have not only sequencing of…, not sequencing of her tumor but sequencing of her regular genome to see could there be any hints about, you know, myeloma genes and…, and it will take… because its uncommon and because sequencing is not readily available to everyone, this is probably some years down the pipe, but perhaps we will get to a point where there may be a myeloma gene or…, or predisposition identified.

Matt Goldman – Okay. Yeah, and I guess, just to thank you. I was just…, to add on to that, it came to my mind, it…, it would be interesting to know outside of genetics versus environmental factors, what things are people exposed to? Can we differentiate between things that…, that environments that people live in, what may have some sort of, say some sort of role in even becoming smoldering. That can be…, that's more like an academic exercise versus something that MMRF researchers are doing.

Anne Quinn Young – Oh, that's…, I mean its definitely epidemiology and I…, I do… There obviously have been things like Agent Orange that have been associated with not just myeloma but other blood cancers or very extreme exposure to the world, being first responders to the World Trade Center, but…, and then certainly in other disease there are these cancer clusters and there have been some research. I know Mayo and I think, at least Mayo has looked at, again you are back to hereditary but at least in families which could be hereditary or could be that common environmental exposure. So, its not passive genes, but everyone lived in the same town and was exposed to something. You know I think there are some anecdotal discussions, but I have…, and people have come to me at the foundation and we pass them on to some researchers, but again the numbers are so small that I don't think anything yet is really…, again aside from really extreme exposure like the atomic bomb and Agent Orange, there haven't really been definitive exposures defined.

Matt Goldman – Okay. Thank you.

Gary Petersen – Thank you, Matt, and what we would like to do now is go to Pat Killingsworth. Pat said he wanted to bat cleanup. So, Pat!

Pat Killingsworth – Thanks, Gary. Hi, Anne. I didn't see you at ASH this year. Sorry, I missed you.

Anne Quinn Young – I know. I… You know I was there very, very briefly, but it really is…, Pat, its awesome to hear your voice because I know you had some challenges lately, so its…, its great to hear you.

Pat Killingsworth – Yeah, I was the guy hiding behind that mask and hat. (Laughter) So… Could you…, could you run through, I…, I mean it…, it was… it went so fast. So, when you started talking about a couple of the new inhibitors and…, and several from the new drug classes, could you…, could you just back up and, I mean which of these drug classes do you see… Are any of them going to be as important as proteasome inhibitors or IMids, I mean do you see one of these other classes emerging as having that amount of impact?

Anne Quinn Young – You know you are…, you are asking like Jack with the crystal ball and, you know, and certainly and…, and not from a scientist or…, or clinician either. You know what I would say is and…, and don't forget steroids too because as…, as much as I think a lot of people would like to see steroids go away. They still seem to be part of that…, that backbone. You know its…, its really hard to say, there really, there haven't been many agents that have single, any single agent activity. Even IMiDs don't really have much single-agent activity, at least when there is active disease, not the maintenance setting. So, I think some of these antibodies… You know the daratumumab has had single-agent activity in heavily refractory patients and has the benefit of not…, and some of these other antibodies as well, not having overlapping toxicity. So, they don't… You know they…, they are not causing lower blood counts and…, and GI issues and then some of the other things that you see with proteasome inhibitors or…, or conventional chemo. So, I think those…, perhaps there could be classes of antibodies, they could be anti-CD-38. It could be the anti-CD-38, ones that could become part of a backbone. I think it…, it comes back to what I said earlier and really a focus of the foundation is…, is understanding the right combinations and the right sequences for…, for patients. You know right now, all patients are treated more or less upfront with these broadly active treatments. There is nothing particularly targeted and maybe…, maybe that…, that will be the main theme, or maybe it won't be, but in order to have it….

Pat Killingsworth – So, if you could help which drug to give to which patient and when… I get it and…, and I am sure the daratumumab to the world, I was thinking more of these checkpoint inhibitors and all of that… I mean people start getting excited about some of these things… I just… I just wanted to…

Anne Quinn Young – Its so…, you know, its such… Yeah, I think its early days again. I…, I mentioned that within the MMRC that.., that PD-L1 antibody trial has enrolled. Its…, its both in…, in early relapse but also in patients who are very, very early relapse often with stem cell transplant. You know it…, its been enrolling really quickly, so clearly there is a lot of excitement. We don't have any data yet, but I think it goes back to having these treatments that don't have the same kinds of toxicities. You know some of these other broader classes like the HDAC inhibitors, the Selinexor one that could have broader applicability. They are not targeting a specific mutation. Its just…, its early days. I couldn't even say what the next class of drugs that would be approved could be, but we are really looking a lot at in terms of large classes for the antibodies and then for patients who have specific mutations, do some of these molecularly targeted agents really make a difference.

Pat Killingsworth – Sure and I am sorry for putting you on the spot and its not…

Anne Quinn Young – No.

Pat Killingsworth – You are just so…, you are just so close to it. I know it isn't specifically…

Anne Quinn Young – Yeah.

Pat Killingsworth – …your area of expertise, but how about…, how about patient quality of life? I mean the way you guys are branching out… By the way, your website, I was talking… I was…., I was on the site and its…, its so easy to, it looks like to…, to get up to talk to one of these counselors. Are these nurse counselors? It really…, it really works nice on…

Anne Quinn Young – Oh, thank you. Yeah, we…, we…

Pat Killingsworth – But how about patient quality because its not that the oncologists don't care and the hematologists don't care, but, you know, when we are living three and four years, I was wondering, but now as…

Anne Quinn Young – Yeah.

Pat Killingsworth – …as we are living 6 and 8 and 10 and 15 years, you know, quality of life takes on a whole new meaning and I just wondered if there…, you know, if the MMRF is doing anything as far as that goes?

Anne Quinn Young – You know I think it…, it has to increasingly be part of, you know, just what… Does the strategy of the consideration in terms of what treatments are brought forward, not just, you know, are they affected but, you know, what's the…, the side effect profile and…, and, you know, again I keep…, I keep going back to some of these antibodies but they…, they really, you know, they are…, they are not the most convenient in terms of infusion times right now, but in terms of having some of these side effects that can really affect it, you know, a patient's day-to-day living, they are not present and I think figuring out, you know, really is not only the right combination of sequence, but the right dosing for every patient because, you know, again the disease is heterogeneous and patients, as everyone well knows, tolerate these treatments very differently as well. So, we are…, you know, we are mindful of that and really do encourage patients to be very open as well. Because…, because there are so many treatment options, its…, you know, its okay to say okay, these side effects are just awful and potentially switch to another option. As you said, its not only when, you know, patients are living three or four years. It was also when there are only three or four different treatments that you knew what we could really switch off because then you are risking becoming resistant and you lose an option.

Pat Killingsworth – Sure. Well, I am just waiting for you guys to do something like, boy, do we have an acupuncture…, a key acupuncture spot for you? (Laughter) Or, we have good news on the medical marijuana front…, or, you know… (Laughter) No, I get it, but…, but that is something to think about and that is something that, you know, really isn't being done and…, and like I said, the heme-oncs are not going to do it and family practitioners, general practitioners about all they do these days is coordinate referrals. So, you know, nobody is really…, that would be nice still almost to have a…, just like, let's see, is there room here at the top of your cycle, oh, there is room for another tab or two, like…, like…, like you don't have your fingers in every pie already, but it would be…, it would be interesting to…, to, you know, branch out a little bit and…, and think about ways that we can…, that would allow us to function better. You are right. If…, if there is less toxicity and if the drugs match up better, there would be less toxicity. Its just not as fun as me inviting you down to the beach party and people or something, you know, let's havea little fun with this thing.

Anne Quinn Young – Yeah, I mean but I think too, you know, perhaps CoMMpass can start to shed light on, okay, these…, these patients are expressing, you know, awful bone pain. You know, it…, you know, are there…, you know mutations are signatures that, you know, can predict those patients early on before that bone pain starts and…, and do something to prevent it, I don't know. I mean this is very, you know, I am talking to myself conceptually, but, you know, I do think hopefully we can learn from patients and…, and understand why one patient may have certain symptoms versus another and are there…, are there ways again to prevent that from becoming such a huge issue.

Pat Killingsworth – Sure. Well, you have a… I know you have a wonderful family and you don't have a life because you have given your life basically for patients like us and I want to thank you for that, but I…, I think they still remember about you. I just… I posted a picture of you on my…, on my blog today. I got a late start, but its like a…, its like a realtor. Have you ever noticed the realtors? They… Their pictures are all like 15 years, almost look like high school graduation photos, that's sort of what your photo looks like.

Anne Quinn Young – Okay. I'll go… I'll go check it out. Now, I am curious.

Pat Killingsworth – You're looking good. I just know you are still 28. That's good.

Pat Killingsworth – Thanks. Thanks for all you do. Thanks, Gary.

Anne Quinn Young – Thank you, Pat.

Gary Petersen – Yeah. Thank you, Pat, and I hope you will feel better.

Pat Killingsworth – Yeah, but she just can't be that bad if I can get around like this, right?

Gary Petersen – Well, I…, I don't know. It…, it may be, we don't know…, we don't know where you are sitting right now.

Pat Killingsworth- That's too…, that's too close to the truth there, Gary.

Gary Petersen – Priya, how about some of the callers?

Priya Menon – Yeah. Thank you, Gary. Listeners, if you have a question for Anne, please press 1 on your keypads and let us know. We will bring you on air to ask your question. Meanwhile, Anne, we have received some questions from our listeners on our website. We will just go through them. Yes. The first one is, does the MMRF support early intervention in those with smoldering multiple myeloma? If so, can you elaborate and provide specifics if there is an…, if there are MMRF clinical trials in development?

Anne Quinn Young – Yes. So, perhaps, this question came in before I covered it. We do have through our clinical research network, the MMRC, two clinical trials right now open for smoldering patients, one which is daratumumab or Darzalex, the antibody that was approved at the end of the year and then one that elotuzumab or Empliciti plus Rev-dex and both are open at several different centers. If you log on to myelomatrials.org, you should be able to see the sites for those or you can call our patient support center at 1866-603-6628 and get more information about those trials.

Priya Menon – Thank you, Anne. The next question is, how long will be it before we can see some reduction in the cost of these new myeloma drugs?

Anne Quinn Young – All these crystal ball questions! You know, that…, that certainly is a really, really important issue and, you know, where we…, what we really set our focus is on on value and another, you know I didn't outline as one of our strategic priorities if you will, but it is an area where we do…, we are…, that we are thinking about it and how might we use our data again to better identify specific patient populations, most likely to benefit. I mean, we may find again in…, in that there are certain patients who, you know, only need two treatments upfront and, you know, a proteasome inhibitor IMiD and a steroid and then they may and we could predict them by their molecular profile. Well, that certainly would cut the cost in terms of a triplet, you know, unnecessarily treating patients with a triplet. So, we will be looking at the data to see how this can help in that conversation and then certainly working with different constituents including payers to start to better address some of these issues, particularly if the patients are to live longer, you know, it does…, it does seem that perhaps some of these costs aren't going to be sustainable in the long run.

Priya Menon – Thank you, Anne. Gary, I see you have a couple of questions more. Maybe we could just wrap up with those if you wanted to ask them. Yeah.

Gary Petersen – Okay. I will be happy to. Thank you. Actually, I have another one, which I think is a little bit more important and that is, you…, you talked about smoldering and some of the things that are associated with smoldering and I had recently read an analysis of, I guess if you go to provide your blood and, you know, and they find you have MGUS, they don't accept it. So, they looked at history of that and determined that about 1% of all the people have MGUS or smoldering myeloma, who I guess would be MGUS and then they looked at how they progressed, but 1% of the population in the United States is 3,500,000 patients. So,

that's a lot of folks with MGUS and that could potentially, you know, progress to myeloma and…, and then another study was in blood that they did for zoledronic and denosumab. Its the blood thing and it shows that of those patients, they got about…, about 12% are found in phase 1, ISO staging; about a quarter or 25% are found in stage 2; and the vast majority or 60% are found in stage 3. So, if we can just find it early, you know, we would…..have all these issues with kidney damage and all those things and…, and catch it before, you know, so you can watch during the MGUS phase, but is there anything that you guys are doing at the MMRF that looks at early diagnosis and methods of early diagnosis or at least finding it before it…, it ends up with end-organ damage which is why people go and why…, why they find it in the first place.

Anne Quinn Young – So, we…, we completely agree and certainly that's why to start some of these trials in smoldering patients with, you know, treatments that don't have significant toxicity tend to delay the progression of the disease. We are also… There are, you know…. Our investigators in our team here are considering, you know, back to your point about MGUS patients, there are…, there do seem to be some, you know, some consensus around predictive factors for that 20% of MGUS patients that will progress to myeloma and do we, you know, do we not just do trial for smoldering, do we do a trial in those high-risk MGUS patients? You know the other thing that we have that, you know, we really, you know, the resource that…, that we have to figure out how we use this knowledge through CoMMpass to qualify, patients can't have been on any treatments yet. They have to be newly diagnosed, but they need active myeloma that requires treatment. So, you know, we had a number of "screen failures" for CoMMpass and those were predominantly MGUS or smoldering patients. So, you know, we do have samples…, some samples from patients who were "screen failures," so they are not part of CoMMpass if they didn't progress during the…, the enrollment time and really, you know, again talking about how we look at those resource potentially to see if, you know, there is any…, any insights to be gained in terms of predicting again who may be more likely to progress and then, you know, targeting those patients for trials.

Gary Petersen – Your logic would tell me that, you know, given, you know, phase… There is an analysis that says, you live three times as long if its found in stage 1 than if you find it in stage 3, so that if you find it in stage 0 or before it even starts or smoldering or stage 0 which is MGUS, you know, maybe…, maybe its even greater, you know, if you look at what…, Columbo did the study or is it San Miguel I think who did the study of using Revlimid-dex on...

Anne Quinn Young – Right, yeah.

Gary Petersen – …on high-risk patients and he found out that that the high-risk patients using Rev-dex lived twice as long as those who were watchful waiting and then…, and then…, and then treated. So… …you know, finding it early and nipping it in the bud seems so logical unlike…

Anne Quinn Young – There's no…, there's no question…, there's no question the disease… I mean I think, you know, we all see how resistant its become but, you know, the longer the relapses that the patient has.

Gary Petersen- Yeah. You are getting when its a scratch or… Do you treat it when its a scratch or do you treat it when it…, when it becomes gangrene, you know?

Anne Quinn Young – Yeah, exactly.

Gary Petersen – All right. Well, that was my question and thank you so much, Anne, for all that you do. I'll turn it back over to…, to Priya.

Priya Menon – Thank you, Gary. Thank you, Anne. It was great listening and learning. Hopefully, 2016 will continue with last year's run and bring more positive results for myeloma patient community. I thank the myeloma panel who have been always wonderful as always. Please visit myeloma.trialx.com for myeloma clinical trials. Today's talk will be made available on CureTalks' website along with its transcript. Curetalks.com will have details of upcoming talks. Thank you, everyone.

Gary Petersen – Thank you.

Anne Quinn Young – Thank you so much.

Gary Petersen – Thanks, Anne.

Anne Quinn Young – Take care.