ATLANTA AREA MULTIPLE MYELOMA SUPPORT GROUP, INC.

Northside Virtual MM Support Group

January 6, 2024

Next meeting: Saturday, Feb. 3 at 11:00 AM. Review this year's ASH 2023 recap session with the Emory team.

Business and News

Special thanks to **Charise Gleason** for organizing and hosting the ASH 2023 Recap session with the Emory myeloma experts. Charise has worked with the Winship myeloma program and Dr. Lonial for 20 years. The Winship team has been meeting with AMMSG (Atlanta Area MM support groups) for 13 years to review updates on myeloma treatments presented at the annual ASH (American Society of Hematology) conference. Eight myeloma speakers were a very small representation of Emory's large myeloma program. The meeting was held virtually by request of the doctors due to the recent increases in influenza and Covid cases. There were over 50 people attending online.

2023 ASH Recap Presentation

Here is the short version of this year's ASH 2023 Recap presentation from the Emory Winship myeloma team. Review the newsletter summary and agenda topics listed, then refer to the full set of notes (file attached) for more details on specific topics of interest. The notes are organized by agenda topics.

Agenda

Welcome and Clinical Trials 101 – Charise Gleason, NP, and Bryan Burton
Precursors MGUS+SMM to Myeloma – Dr. Vikas Gupta
Newly Diagnosed MM – Dr. Nisha Joseph
Relapsed MM Trials – Dr. Ajay Nooka
Emerging Insight from Immune Studies – Dr. Madhav Dhodopkar
CAR-T – Dr. Jonathan Kaufman
Bispecifics – Sara Scott, PharmD

Wrap-up and Closing Remarks – Dr. Sagar Lonial

Welcome and Clinical Trials 101 – Charise Gleason, NP, and Bryan Burton

Charise Gleason opened the session with a review of clinical trials.

Phase I – to determine the appropriate dose for further evaluation. Find a safe dose, decide how the agent should be given, and observe how the agent affects the human body. Average participants enrolled is 15-30.

Phase II – To determine whether an agent has activity against a specific cancer. Using phase I dose, test effectiveness of the drug in a larger population, usually < 100 and gather additional safety data.

Phase III – To determine whether a treatment is effective. Enrolls more patients, 100s to 1000s, at multiple locations around the country. Compares Clinical trials to current standard of care (SOC) treatment.

Phase IV – Post FDA approval, various goals.

Brian Burton noted the extensive staff available to support clinical trials. Now that they are fully staffed, they are expecting an increase in patients enrolled in clinical trials. Important facts to know about clinical trials:

- Participation is voluntary
- You will not receive a placebo
- Your health and safety will always be a priority
- You may discontinue at any time

Precursors MGUS+SMM to Myeloma – Dr Vikas Gupta

Dr. Gupta talked about understanding the risk of MGUS or SMM advancing to full myeloma. One study is looking at the labs of SMM patients at the time of diagnosis and again one year later. It is not clear at the time of diagnosis how long the patient has had this disease and is the testing being done at the beginning of their disease or at a point where they are about to progress? Researchers looked at the changes in labs over that year and tried to extrapolate data into a risk stratification score that could more accurately predict progression to MM. Once a patient is determined to be high risk, what are the interventions? There are more aggressive trials, called curative intent trials. Then there are those trials that are less aggressive. A new approach is incorporating bispecific antibody, Teclistamab, in high-risk SMM. Which

approach is the best is still a matter of a lot of debate, but toxicity should be taken into consideration. There are more trials ongoing at Emory.

Newly Diagnosed MM – Dr Nisha Joseph

Dr. Nisha Joseph spoke about newly diagnosed myeloma. This is actually a big year for those newly diagnosed at ASH. There were two large, randomized phase III trials presented. Emory also had the opportunity to present our own data, which is exciting for us but hopefully for you all as well since this demonstrates how well our patients are doing, which is exciting and rewarding. The Perseus trial looked at RVD vs. RVd with Dara – four cycles followed by transplant and consolidation. Then both groups went on maintenance. One of the concerns with adding Dara upfront is if patients are still going to be able to collect stem cells. Studies were done to look at that question. The results showed that adding Dara upfront extends PFS without significantly increasing side effects. Emory started using Dara with RVd for induction in 2018 so there is real world data from those patients. Dr. Joseph was able to present this at ASH. She noted that about 35 to 40% of the patients in the study are Black, which is higher than what is seen globally in clinical trials. The results also showed that the depth of response was higher with Dara RVd. They are also showing longer overall survival at almost 11 years, which is fantastic. She said that there was not a big difference between Black and White patients. That means that if you give patients the same access to care, they have the same outcomes.

Relapsed MM – Dr Ajay Nooka

Dr. Nooka presented on managing relapse. We have seven classes of drugs altogether. As of today, we have 15 new drugs that are approved. If you take the available options, the number of drugs available is exactly 25 based on the NCCN guidelines. *So how do we choose a regimen?* Treatment options consider what the patient received before and what adverse events has the patient suffered because of their previous therapies? All risk factors are taken into consideration before choosing one of these platforms. *The best choice that is right for you is the discussion that your physician and you should be having to decide that right option.* Dr. Nooka reviewed clinical trials of two drugs vs three drugs and always wants a triplet to gain better mileage after a

relapse. Then he talked about the next generation of IMiDs after Rev and Pom. Also, high risk patients with translocation (11;14) are getting great results with Venetoclax. Sonrotoclax is the next generation after Venetoclax and it is showing great results in trials as well.

Emerging Insight from Immune Studies – Dr Madhav Dhodopkar

Dr. Dhodapkar talked about the newest research in immunology beyond CAR T and Bispecifics. Emory research is showing that tumors grow in a clustered fashion and there are many patterns in which the tumors can grow. Another point to understand is that as the tumors progress from MGUS to myeloma, the immune system weakens in the great majority of myeloma patients. The degree to which the immune system weakens differs in individual patients, irrespective of genetics. The question to ask is *how does this impact treatment outcomes and the difference in survival rates?* The third message that we are learning from multiple groups now is about T cells, which have been the major workhorse of immunotherapy, including in myeloma, both in the context of CAR T cells, as well as Bispecifics. T cells could get tired over time, some more than others. The word "tired" means that the T-cells become less and less functional. Some adjustments may need to be made. Finally, the tumors continue to play like hide and seek with immune cells as we continue to treat them. This is becoming evident with acquisition of mutations or alterations in tumor cells that specifically alter the target that we are trying to hit with the bispecific antibody or with CAR T cells. That is going to mean that we need to think about either multiple targets or combinations of different treatments. These are some of the main themes in the preclinical studies from ASH that we will hear about in the future.

CAR-T – Dr Jonathan Kaufman

Dr. Kaufman reviewed data about using the already approved CAR T therapies earlier in treatment. First is the KarMMa 3 study. Ide-cel *(Abecma)* is currently approved for fifth line therapies and beyond. This trial looked at patients who had two to four prior lines of therapy. The study was using Ide-cel versus five different options of standard of care (SOC), treatments used in the clinic every day. The PFS showed significant improvement with Abecma. There was no difference in overall survival (OS)

for the entire group, if they received CAR T therapy earlier or got the CAR T cells one line later. Cilta-cel or Carvykti is the other approved CAR T cell therapy. The Cilta-cel study designed the CT trial a little bit differently. For Abecma, there are two to four prior lines of therapy for CT eligibility. Cilta-cel is one of three prior lines of therapy. So, it is available notably earlier than the KarMMa 3 study. It also included a slightly different patient population. Just like the prior study, a clear improvement in the percentage of patients responded to Carvykti versus the standard of care without additional maintenance therapy or any follow-up therapy. 75% of the patients have no progression of their myeloma (PFS) after two years. The data suggests thinking about moving CAR T up earlier in the course of therapy.
Carvykti and Abecma target BCMA. BCMA is also the target of Blenrep in clinical trials and the same target in some of the Bispecifics. There are other targets to consider. now have a bispecific antibody GPRC5D treatment with talquetamab and this is looking at CAR T cells using this new target. This trial had different side effects than the BCMA targeted treatments. They are doing everything we can do, from dosing and timing and supportive care, but none of it is severe or long lasting. Most of it resolves within the first month.

Bispecifics – Sara Scott, PharmD

Sara Scott, PharmD, is the newest member to the myeloma team. She joined the team back in May as the new clinical pharmacy specialist. Bispecifics are immunotherapies that utilize your own T cells to attack and kill the myeloma cells. They use two FDA approved targets on the myeloma cells which are BCMA and GPRC5D. There are more treatments in the pipeline that use other targets. The CAR T process can take some time and it is not appropriate for every patient. There are a lot of toxicities to consider and other complications. Bispecific antibodies provide an alternative option that are readily available "off the shelf" and a little better tolerated. Everything with the bispecific antibodies is phase I and phase II data or real-world data. There is no randomization or direct comparison to our other myeloma therapies. Teclistamab was approved based on the findings of the MajesTEC-1 trial which showed an overall response rate of 63%. The real-world data includes patients who may not qualify for clinical trials due to comorbidities or other complications. Beyond efficacy, it is important to know about side effects. The

biggest side effects seen at Emory concerning CRS, cytokine release syndrome, is a fever that could get worse and lead to a severe infection. The next bispecific antibody is elranatamab or Elrexfio, which was approved in August. The overall results were good. Patients who had achieved a complete response (CR) or better and were MRD tested, 90% were MRD negative, which suggests a really deep response with this medication, and hoping it will help the response last a long time. This is impressive news.

The third bispecific antibody to highlight is talquetamab or Talvey. There were a few updates for this medication at ASH. This is a bispecific with GPRC5D targeted on the myeloma cell and it was also approved in August of last year. It is typically used after patients have had BCMA-directed therapy, whether that is a CAR T or one of our other bispecific antibodies. The results presented at ASH gave information on decreasing the dosing interval and also treating in combination with pomalidomide. The overall response rate in this trial was high at 66%, which is wonderful. Pomalidomide can keep those T cells working so that talquetamab can continue to kill the myeloma cells.

The last piece that Sara highlighted on the bispecific antibodies was the data that Emory had the opportunity to present at ASH on the use of Tocilizumab or Actemra to prevent the cytokine release syndrome. At Emory, we explored the use of Tocilizumab to prevent CRS with the ultimate goal of administering those step-up doses of bispecific antibodies safely in the outpatient setting, thus preventing hospitalization and allowing patients to be comfortable in their own home on therapy. What was observed was patients who did not receive tocilizumab showing CRS symptoms at 72% compared to only 26% of patients who were having CRS while given tocilizumab dosing. A pretty big reduction in the incidence of CRS. The other note to point out is that in those 26% that did have CRS, the vast majority only had grade one, which means they only had a fever. There were none of those other complications of CRS such as blood pressure or breathing changes. So, it is not only preventing CRS but making it less severe. Sara's final comment was that there are a number of interesting drugs in the pipeline. Some of the new compounds had some data shared at ASH and these are all in the family of T cell redirecting therapies. There are three new BCMA Bispecifics and a tri-specific! It targets BCMA on the myeloma cells and CD3 on the T cells and they have added a

third arm to make this the "tri" to target CD 38 which is the target of daratumumab so it will be exciting. More to come at the next ASH.

Wrap-up and Closing Remarks – Dr. Sagar Lonial

Dr. Lonial wrapped up the session with an Emory overview. We heard from many of the Emory team here, who are leaders in the field, not just at Emory, but at the national and even international level. Some perspective for those of you who are on this call, the Emory myeloma team wants you to feel like *this program is your program*. We are here because of all of you on this call as well as many of you that are not on this call. Emory and our myeloma program is bigger than the city of Atlanta, bigger than the state of Georgia. This group has people fly in from all over the world to get our opinion and give treatment recommendations to other physicians so that they can execute the highest-level of care like what you heard from Dr. Joseph and other situations like that. So just to give you a sense of the program outreach, we will see roughly 4,500 myeloma patients this year. That makes us one of the largest myeloma programs in the world. As Charise and Brian and others mentioned at the very beginning, there is no drug in the last 20 years that has been approved that was not available at Emory first.

Dr. Lonial went on to answer questions.

Question in the chat about defining BCMA which stands for B cell maturation antigen. It is a receptor on the surface of all plasma cells and thus it makes a good target. It is also an important signal for survival of plasma cells. So, interrupting the signaling by binding with a virus, specifically an antibody drug conjugate or a CAR T cell, inherently makes the myeloma more sensitive to everything else that we do.

Q: A question in the chat has to do with the use of dex and whether we are looking towards reducing the dosage.

A: So, in terms of dex, I think we have already made substantial changes in terms of dosage. As much as everybody keeps sort of killing dex, dex is really good at killing myeloma. Dex is also really good at doubling the efficacy of pomalidomide and Revlimid and Iberdomide and Mezigdomide. They are effective drugs, and our approach has been in the last few years to talk about the duration of dexamethasone. We are not using it at 40 milligrams a week

forever. Many of the trials still have it that way, but I think many of our patients start to taper after they have seen a big response. Typically, even in the maintenance setting, we have patients off their dex between 6 and 12 months after starting maintenance, even for high-risk myeloma. So, age certainly plays a role in dex dosing, but it is more about duration of dex as opposed to the absolute dose of dex.

Q: The second question was about where does stem cell transplant fall in treatment plans.

A: If you look at the median progression free survival after a transplant for all patients, it is five and a half years. The longest PFS we see after a CAR T cell is three years. So right now, I am not convinced that CAR T is going to replace transplant. There are trials ongoing that are asking that question about whether you can replace transplant with CAR T. They are using limited duration maintenance in both arms there so I do have some concerns or hesitations about what that trial is going to ultimately show, but that is really the data we need to understand whether CAR T can replace transplant. As I said years ago when we were talking about can conventional therapy replace transplant. My goal is not just to be as good. So, if you do something and you are just as good as a transplant, there are a lot of quality-of-life issues in the long term that a transplant may be better for. You know, the two months post-transplant period is the quality of life is not as good, but after that you are just on single agent maintenance. Whereas if you are on triplet or quadruplet therapy for two or three years, that's not easy therapy to take, and it is certainly not cost effective. So, the transplant question is going to be here with us for a while and we continue to recommend early transplants to almost all of our patients.

Q: There was a question about stress, inflammation in myeloma.

A: We know that inflammation does trigger certain immune activation that may limit the efficacy of immune based therapies. Again, dex is important as an anti-inflammatory. So, it is one way to talk about trying to combat that.

Q: There was a question about dental issues in myeloma therapy.

A: With the bisphosphonates, the ONJ ends up being about 3% or 4% of patients. But we are using less bisphosphonates for shorter periods of time now that we are achieving deep responses with quadruplet-based induction

and transplant consolidation. So, my hopes are that ONJ will continue to be less and less of an issue over time as well.

Meeting Minutes

Southside Virtual MM Support Group

January 27, 2024

Next Meeting: February 24, 2024 – *All You Want to Know about Bispecifics and Daratumumab*.

Presenter: Kim Y. Burney, BSN, RN, MSNed, OCN Educator, Johnson, and Johnson/Janssen Pharma

"For Men (with myeloma) Only" – Tuesday, February 27 @ 6:30 PM – *Communication with Health Care Providers: From a Man's perspective*. **Presenter: Brandon Blue**, MD, Moffitt Cancer Center, Tampa

Business & News

Thank you to **Gail M** for hosting the January meeting. The meeting opened with a moment of silence led by **Doris.** Our speaker, **Ms. Burney**, was unable to be present due to a family emergency. She has rescheduled for the next meeting on February 24. A special thanks to **Nancy Bruno**, Regional Coordinator for IMF Support groups, who was available to share her knowledge and information on *Bispecific*s. We were also excited to have a visitor; **Robyn Cornell** joined us. Robyn is a member of Doris' NPU. She is also the talented person who provides our reminder calls each month, sharing the upcoming agenda and how to join the meeting.

Guest Speaker Presentation

Nancy B. spoke about new treatments and CAR-T as an additional treatment option. Jannsen handles CAR-T, Bispecifics, and Darzalex therapies. The talk started with a review of definitions; Bispecifics, BCMA, CAR-T, and side effects

like cytokine release syndrome (CTS). Nancy formed some parallels between myeloma and the language we learned from COVID-19 (cell variants, CTS, COVID cell graphic) for greater understanding. She also displayed a chart of the new myeloma treatments and classes of drugs being used and pointed out what drugs Jannsen has approved. Thank you, Nancy, for being an excellent teacher and being prepared with this information. This will help us have a better foundation in understanding Bispecifics when Ms. Burney presents in February. Following Nancy's presentation, a series of short videos featuring Dr. Joe Mikhael was reviewed for more education on Bispecifics.

Group Discussion

Suggestions on new presentations for Southside Support Group meetings were discussed. One suggestion was strength training for myeloma patients. This is important for everyone's overall health as we lose muscle mass as we get older. Additional caution is necessary for those with myeloma since bones are directly affected by the condition itself. *What can we learn from hardcore weightlifters, bodybuilders, gymnasts, and others?*

Popular meeting topics in 2023 included: *Understanding kappa vs lambda light chains? When is the best time to take Dex and deal with the symptoms? What should I eat to support my nutrition needs and treatment? What is the prognosis of someone with MM?* and *What are CRAB symptoms*?

Special interest Support Group available: *IMF-myeloma.org* – High risk, smoldering, Myeloma families with young children. *Healthtree* special interest group for high-risk group with (11;14) translocation

Dr. Jennifer Rooke has begun a 12-week session of workshops on Whole Food Plant based eating. These are virtual meetings held on Wednesday evenings, 6 – 8:00 PM. Optimal Health and Wellness Workshops

"For Men (with myeloma) Only"

Ted shared that the men had an excellent time at their January 23 meeting. There was a great conversation, and it was an open, active group. He urged the other men to join the group for an hour once a month and share your

myeloma journey. Dirk underscored Ted's comments and said it was a good time with "guys sharing guy things."

March is Myeloma Awareness/Action Month – *You are not Alone*.

Share myeloma information and resources. Send out an Eblast and flyers for those within a 250-mile radius. Post information in the health section of newspapers, in cancer centers, infusion centers, neighborhood planning units and more. For more Action, click here - Myeloma Action Month

Patient Update

Alisha had a SCT (Stem Cell Transplant) in June 2023. Chemotherapy has been repeatedly scheduled since then, but Alisha has been too ill to begin maintenance treatment due to pneumonia three times in the past three months. The group asked about her immune system, WBC (White Blood Cell) count and discussed IVIG (Intravenous immunoglobulin) treatment to help boost her immune response. Emphasis on nutrition – and being sure to focus on fruits, vegetables, and a nutrient dense eating plan. Alisha sees Dr. Hofmeister at Emory and another doctor at Grady. **Ted** is doing better and able to turn his head left and right without so much pain. He is recovering following surgery on his neck from a fall off his riding lawn mower. **Cynthia B.** received a SCT followed by CAR-T that responded for about 8 months. She was on Cytoxan for over 2 years until she acquired a lung infection. She was not given IVIG by the decision of the coordinator. Cynthia had a second transplant then developed extramedullary myeloma (collection of myeloma cells that grow outside of bone marrow, making soft tissue tumors). At this point doctors are watching and waiting. **Wanda P.** shared that she remains vigilant in fighting germs and possible infections. Each doorknob in her home has a mask attached in case deliveries or visitors arrive and she wipes down surfaces regularly. Wanda is 67 and has been vegan since age 20. She has tried 4 different times to harvest cells for a SCT at considerable personal expense (~$8,000) she found out after the fact. **Alma** was on a Bispecific clinical trial that did not work for her, so it was discontinued. **Sandy B.** shared she was approved for assistance and that funds were retroactive back to the date of submission. Be sure to submit from your doctor that you are still under active

treatment. **Frank** and **Fran M**. were both fortunate to receive a $5,000 grant from LLS. **Glenn** found a website that showed when funds become available – he will search for the site and share with the group. **Portia** shared that a few members have received funds from her foundation, **Every Color Matters Awareness Foundation** (ribbons representing different cancers). She encourages others to apply for the funds with a stated need (https://www.everycolormatters.com/). Both Pat C. and Veronica H. have benefitted from Every Color Matters funding. Both uninsured and underinsured are invited to apply. Their annual Gala is June 24 at the Delta Flight Museum.

Veronica M. shared that her father died in 2019 from myeloma in South Carolina. There was no diagnosis after several months of symptoms. In the last 3 months of his life, he lost a great deal of weight. The family was finally informed that he had MM. Veronica has learned more about what took her father away. This is yet another example of the importance of sharing the myeloma message to communities and to ask their doctors to look for myeloma. Early warning signs include excess **calcium** in blood tests, kidney (**renal**) failure, unexplained fatigue or **anemia**, **bone** damage/back pain – **Myeloma CRAB** criteria.

Respectfully submitted,

Gail M.