ATLANTA AREA MULTIPLE MYELOMA SUPPORT GROUP, INC.

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Meeting Minutes
Northside AAMM Support Group
January 6, 2021

The January meeting was our annual ASH review with the Emory Winship Team. We had over 70 people at the virtual meeting for exciting information on new treatments.

Charise Gleason opened the program with explaining clinical trial phases: Phase I is a small group (15-30) trying to determine the maximum safe dose, how the treatment is given, and side effects; Phase II is a larger group (< 100) working to define the effectiveness of the dose that was decided in Phase I and how patients respond to therapy; Phase III includes hundreds to thousands of randomized patients and the outcomes are compared to standard treatment.

Shondolyn Richburg, CCRC, Clinical Research Coordinator, told us about the myeloma clinical trials at Winship. There are 44 studies open to accrual, 54 studies closed to accrual, and 17 studies in the pipeline. She said that patients can participate through referral from your clinical team, referral from your local physician, or self-refer from www.clinicaltrials.gov This web site is difficult, but you can find who the investigators are and contact them. The Winship web site has a listing of their trials at Clinical Trials Office at Winship | Winship Cancer Institute (emory.edu) You can also check out the Myeloma Matrix from IMF at Search clinical trials | Smart Patients. When reviewing a clinical trial, understand the drug and side effects, ask about costs, talk to family, do your own research, and prepare your questions. Ask about options, why you would be good for this trial, what is the schedule, and read the protocol for the full information. Once you apply, there will be screening to see if you are eligible. Important points to remember:

- Clinical research is always voluntary. You can stop at any time.
- You will not be charged to participate.
- Visits may be conducted by your original clinical team or their colleague.
- Your health and safety are always a top priority.

Dr. Lonial commented that there are so many great things that they are seeing in their research and they will only open a clinical trial when a new treatment looks very promising. The COVID virus did not slow down clinical trials. 109 MM

patients were included in clinical trials in 2020. Winship appreciates the trust that patients have in their trials.
Q - How else can I become educated about clinical trials in general? **A** - Once you start a discussion with your doctor, they will assist with your education. Emory is very selective about the trials that they open and will not open a trial unless they believe that there will be good activity against myeloma. Even if you are being treated elsewhere, Emory can help direct your care and provide you with information about your options.
Q - What does median OS not reached mean? **A** - This is an optimistic statement. In clinical trials, median survival refers to how long patients survive after a certain treatment. When median overall survival is not reached in a clinical trial, it is because more than half of the patients were still alive when the trial was reported or concluded. Contact Shondolyn.k.richberg@emory.edu if additional questions.
Dr. Nooka talked about the treatment journey. The initial phases vary for those eligible for transplant vs. those not eligible. If eligible for transplant, the phases are: Induction, Consolidation (transplant), then Maintenance. For those not eligible for transplant, the phases are: Induction followed by continuous treatment and managing refractory disease (when MM progresses during treatment). Dr. Nooka showed statistics from 1000 patients over more than ten years for those who received RVd induction therapy. It showed a median PFS of 65 months and median OS of 126 months. The "median" number represents the middle of the group where half are above and half are below this point. The results shown are incredible numbers for patients as remission and survival continue to improve. This also shows how clinical trials are benefitting all patients.
He then talked about factors to consider at relapse:

1. Patient characteristics: comorbidities, frailty, patient preferences
2. Tumor characteristics: cytogenetic risk, rapid increase in M-protein
3. Prior treatment: response, toxicity
4. Access/availability/transportation and support issues

Note that your input is part of the decision. Of course, clinical trials can be part of the discussion.
Q: For a relapsed patient that has not had a stem cell transplant (SCT), is the first treatment a SCT? **A:** Not necessarily. There are a lot of factors in your entire

health history that need to be considered and this should be discussed with your physician.
Q: Please define high risk and standard risk patients. What cellular markers determine level of risk in patients? A: Patients with abnormalities inside myeloma cells are considered high risk. This includes chromosome deletion 17p; and translocations t(4;14), t(14;16), and t(14;20). There is also additional risk with some patients who have extra copies of chromosome 1q.
Q: Are there new targeted therapies for patients with chromosome deletion 17p?
A: Chromosome deletion 17p is challenging to treat because we are trying to restore an activity that has been lost, specifically to TP53 activity. However, there are investigational drugs such as Idasanutlin that are being studied.
Dr. Kaufman talked about a clinical trial with 474 patients comparing KRd+ASCT vs. KCd+ASCT vs. KCd for 12 months. K = Kryprolis, C = Cytoxan, R = Revlimid, d = dex. For those patients who sustained MRD negative, KRd+ASCT was 68%, KRd12 was 54%, and KCd+ASCT was 45%. PFS at 36 months: KRd+ASCT was 78%, KRd12 was 66%, KCd+ASCT was 58%. This is a lot of numbers and letters, but the bottom line is that a transplant after initial treatment sets the stage for longer remission (PFS). This information is watched by MM doctors and influences their decisions. Dr. Kaufman then provided an update to IFM 2009 which compared RVd alone to RVd then ASCT. Both groups had maintenance of Rev for 13 cycles. The results after following patients for eight years were a 30% reduction in the risk of progression or death in patients receiving transplant (ASCT). The median PFS for RVd was 35 months while the PFS for RVd with ASCT was 47 months, one year longer. Both these studies are testing the value of transplant and the data shows that a transplant still provides significantly better outcomes.
Dr. Kaufman gave an update on the GRIFFIN trial that enrolled patients from 2016 until April 2018. This trial involves transplant eligible newly diagnosed (NDMM) patients given D-RVd (Dara+RVd) vs just RVd before and after transplant. After two cycles of consolidation (60-100 days post-ASCT), both groups got maintenance for cycles 7-32 and the D-RVd arm got D-R while the other arm got just R. Looking at results, responses deepened over time. For D-RVd at the end of consolidation, CR(complete response) was 51% and at the end of 12 months of maintenance, CR was 81%. For RVd at the end of consolidation, CR was 42% and CR was 61% at the end of 12 months maintenance. The D-RVd group was nearly double CR compared to the RVd group and this may lead to FDA approval to give NDMM longer remission.

Dr. Hofmeister talked about the various immune therapies. Chimeric Antigen Receptor T-Cell is CAR T. T cells are collected from patients much like stem cells are collected. They are then engineered to seek a target on the myeloma cells and destroy the myeloma cells. BiTEs are Bispecific T-cell Engagers. These consist of two components where one binds to T cells and the other binds to the myeloma cell leading the T-cell to secrete cellular poison that kills the tumor cell. BiKEs are Bispecific Killer Engagers that engage the Killer Cells in the immune system and link them to the tumor cells to kill them. Antibody Drug Conjugates (ADC) are targeted antibodies carrying a poison. They are sucked into the MM cells and once inside, the poison is released to kill the cancer cell. He related this to a Trojan Horse that is brought into the city and there are soldiers inside who escape at night to damage the city. Good plan! Currently there are five BCMA-targeting Bispecific treatments in trials. There are two others with different targets. Their CR results vary from 10% to 42%. As MM struggles to survive, these tumor cells reduce production of BCMA. There are other bispecific treatments going for two different targets on the MM cells. Dr. Hofmeister reviewed the results of clinical trials with CAR T therapy and several are showing strong response rates, but the results are not holding much over one year. We will keep track of future results.
Q: Who are the best candidates for CAR-T cell therapy? **A** - At this point, CTs for CAR-T exist for patients that have relapsed/refractory myeloma and have progressed on Daratumumab and that have newly diagnosed high risk myeloma. Soon other CAR-T CTs for early relapse will open.
Q: Who is eligible for CAR-T therapy? **A**: There is no age limit. Patients must have good organ function and performance status. Comment from Dr. Lonial: Emory hopes to be making CAR-T cells from scratch within the next four months in the new Emory lab. This will provide eligibility and cost advantages when these cells can be made independently from a third part.
Dr. Vikas Gupta talked about updates on precision medicine in myeloma. He showed a chart of over 50 mutations in MM and most mutations are present in less than 5% of patients. Even in patients that have a particular mutation, not every myeloma cell in that patient may have that mutation. “Druggable” mutations are even less common, in contrast to melanoma (BRAF 52%) or lung cancer (EGFR approx. 27%), as examples. One trial for a BRAF mutation is highly effective in melanoma, but BRAF mutations are present in 4% of MM. This shows that targeting mutations in MM will be less effective for patients. Dr. Gupta talked about resistance to BCMA. Many patients relapse after CAR-T because the T-cells stop working and something about the myeloma changes. Two groups have

shown that myeloma can lose BCMA to evade CAR-T cells. This is also important for antibodies and BiTEs that target BCMA. He then talked about predicting response to Venetoclax using ex vivo (outside the body) testing. Patients with t(11;14) are more likely to respond, but not all do, and some without t(11;14) respond. Ex vivo testing has been found to correlate with long term response. Researchers are using flow cytometry which is readily available for MRD testing. Venetoclax sensitive myeloma has a unique B cell-like signature. This is interesting to recognize and we may learn more about this down the road.

Q: In the past, even before MYDRUG trials, the MMRF has asked that patients request that our cells be shared with them for their database/Precision Medicine research. Has that been accomplished? What are your other thoughts about this?

A: We have had a sequencing effort where we sent patients cells to be sequenced as a research project independently of the MYDRUG trial. When we perform a bone marrow biopsy, we can take extra bone marrow and send it to a lab in Michigan that does the sequencing. This is still very early and investigational. We are not making clinical decisions on this yet but are still reviewing data for research purposes.

Q: Is there a blood test to determine if you have myeloma genetic components?

A: There are serum sequencing tests, but they are not used for myeloma at this time because we do not have the types of precision medicine or targeted therapies for myeloma that we have for other types of cancer, such as lung cancer. We do not think there is clinical benefit to this for myeloma at this time, but there may be in the future.

Kathryn Maples, Clinical Pharmacy Specialist, reviewed the supportive care for the new treatment options. Blenrep, antibody drug conjugate, causes dry eye and blurry vision. Eye exams are done prior to every dose (every three weeks) and eye drops are used to mitigate corneal events. Dose delays and dose reductions improve the side effects, and they are not permanent. Immune-related adverse events (IRAE) are a result of T-cell activation and can affect many organ systems. Steroids help manage IRAE in general. Some specific symptoms can be managed individually, such as hypothyroidism, rash, colitis, etc. Cytokine Release Syndrome (CRS) is a systemic inflammation that occurs due to large, rapid release of cytokines from immune cells. Symptoms include fever, hypotension, myalgia (muscle aches and pains), headache, low oxygen, etc. Severe cases can affect the lungs and kidneys. These occur within hours and up to 14 days after CAR-T therapy.

Q: Are you learning any treatment to help with the side effects that Belantamab has on the eyes? **A**: Dr. Lonial and Dr. Nooka are working with Belantamab at Emory and the eye issues are being controlled well for patients.
Q: Do you need to wait for the eyes to heal before trying a lower dose of Belantamab? **A**: Yes, we would hold treatments until eyes have healed and then resume with lower doses. There is a grading system that is used by the Ophthalmologist to allow for the decision-making of whether to dose or not. For higher grade toxicity the dose is held until the reexamination shows resolved eye toxicity. We have learned through the CTs that you do not lose the response by waiting for healing and the response can be sustained, which is helping us to design CTs by increasing the dosing interval.
Kathryn answered some questions about the COVID-19 vaccine.
Q: Can COVID vaccine make me sick with COVID? **A:** No. The authorized vaccines in the US do not contain the live virus.
Q: Will I test positive for COVID on a viral test after the vaccine? **A**: No. If your body develops an immune response, then you may test positive on antibody tests, but not on the viral tests.
Q: If I have already had COVID, should I get the vaccine? **A**: Yes. At this time experts do not know how long someone is protected from getting sick again after recovering from COVID. Current recommendations are to wait 90 days from your positive test.
Q: Will a COVID vaccine alter my DNA? **A**: No. COVID mRNA vaccines do not change or interact with your DNA in any way. Winship recommends that you receive the vaccine when it becomes available to you. Winship has a clinical trial for MM patients to check immunity at 3, 6, and 12 months through blood draws.
Q: If you get a COVID vaccine through Emory, would the caregiver be given the vaccine as well? **A**: The vaccine is available for patients. If caregivers are also patients at Emory, they will have an opportunity later.

Submitted by Nancy B and Wendy R

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Meeting Minutes

Southside Virtual MM Support Group

January 23, 2021

Get your vaccine as soon as possible: You may be able to get your vaccine where you are treated for Myeloma – Emory, Kaiser, Northside, etc. For those who are **Veterans**, please check to get your vaccine at any of the VA Hospital sites across Georgia Other sites –

Georgia Department of Public Health: https://dph.georgia.gov/covid-vaccine and Mass Screenings (e.g., Delta Aviation, etc.): https://myvaccinegeorgia.com/

Next Meeting: Voices of Patients and Caregivers, Group lessons on Zoom, and Discuss activities for Myeloma Awareness Month.

We started the new year in January with a specialist in the COVID-19 vaccines and vaccine trials who could talk with us about **COVID-19: Vaccine Updates. Facts, Myths, Status and Vaccine trials.**

Guest Speaker:

Lilly Immergluck, MD, MS is a primary care physician and professor at the Morehouse School of Medicine. She is a pediatrician, an advocate of vaccines, a pediatric disease specialist, and Primary Care physician. She is a member of CoVPN (COVID Prevention Network) and is the Principal Investigator of the Novavax Clinical Trial (another COVID vaccine in development) being conducted at the Morehouse School of Medicine site. She is also a member of the Georgia CEAL team (**C**ommunity **E**ngagement **Al**liance to reduce disparities in COVID-19). She is a very busy physician-scientist. We were fortunate to have her.

How do vaccines work? The vaccine mimics the virus or bacteria that causes disease. This foreign body is called the **antigen**. It stimulates the immune system to build up defenses (antibodies) against the infectious bacteria or virus. The Pfizer and Moderna vaccines both use the mRNA platform, which creates the spike protein and develops antibodies against a piece of the virus. The (messenger) rNA has no contact with your DNA and **makes no changes to your DNA.**

The use of viral vectors is not a novel (new) therapy. Both of our current vaccines in use have been approved by the FDA with **Emergency Use Authorization** (EUA). The Pfizer and Moderna Clinical Trials (CT) showed strong positive results on efficacy of greater than 95% that allowed for the EUA. Trials are ongoing for at least another two years, to determine long-term effects of the vaccines. Phase 3 Clinical trials generally last for about two years.

At the time of our meeting, the pandemic was in its third surge – the biggest surge of the pandemic. At that time, there were 415,000 deaths (mothers, fathers, grandparents, aunts, uncles…) in the United States. (*The numbers today (2.22.2021) are 16,235 deaths in Georgia and 500,000 deaths across the United States. This is the population of the city of Atlanta).*

Grim Facts update on COVID-19:

On December 2, hospitalizations from COVID hit over 100,000 in the U.S. In many instances, there were not enough beds in intensive care to take care of those infected. In January, there were so many hospitalizations in Georgia, that there were not enough beds across the city for COVID-19 patients. An adult unit had to be created in Children's Hospital. On January 20, 2021, over 4,400 deaths from COVID were recorded. Fourth year medical students had to be trained to help administer the vaccine to have enough personnel for vaccinating the public. COVID-19 became the leading cause of death in the U.S., outpacing heart disease and cancer.

Corona viruses will mutate. It is normal, but most of the time it is not enough to impact our health status. The concern is if those mutations take hold and begin to create more problems. In the United Kingdom mutation of the SARS-CoV-2 (COVID-2), called time B.1.1.7 variant, the area of the spike protein makes it stickier and more easily transmissible. The South African strain is fast-moving through communities.

For any Clinical Trials, one should make an informed decision when deciding whether to participate. All participants should be clear that even if they sign up for a clinical trial, they can decide not to participate at any time with no negative repercussions.

Six Facts about the Vaccine:

Fact 1. The COVID-19 vaccine will NOT give you the virus. The vaccine was created with no part of the live virus and cannot cause an infection or cause a positive test for the virus.

Fact 2. Quick development of the vaccine does not mean it is not safe. Significant scientific work was done over the decades on the mRNA platform, collaborations that were incentivized by the government and the pandemic, and more sophisticated technology all contributed to getting the vaccine EUA from FDA so quickly.

Fact 3. A COVID-19 vaccine may give you protection against more than one strain. Like all viruses, the SARS-CoV-2 develops small mutations over time. Information to date shows that Pfizer and Moderna may be effective against multiple strains in circulation.

Fact 4. A COVID-19 vaccine will not change your DNA. A COVID-19 vaccine does not interact in any way with DNA. It triggers an immune response that produces antibodies that protect you from getting infected.

Fact 5. A COVID-19 vaccine has not been linked to issues with fertility or miscarriages. There is no evidence that the vaccines cause increases in infertility or miscarriages. Additionally, the post-infection immune response has not resulted in increased infertility or miscarriages. However, there have not been sufficient studies on this population. Studies with the vaccines and pregnant women are currently being conducted.

Fact 6. We know exactly what is in the vaccine. Pfizer and Moderna have published the ingredients of their vaccines for anyone to see. Speculation that the vaccine contains either microchips or tracking devices have been proven false.

Group Questions on Covid-19:

Should you get the vaccine? The clinical trials have been conducted with those with diabetes, high blood pressures, and other chronic diseases. If you are in active treatment for cancer, you should not take the vaccine If you have severe allergies, you should inform the staff, take your Epi Pen with you. There is polyethylene glycol in both Pfizer and Moderna – no latex. With the Novavax, the trials are conducted with high-risk patients and it has worked for them so far. People with immune system problems and cancer patients should have conversations with their specialists. Getting the vaccine will be on a case-by-case basis.

How often will we have to take the vaccine? At this point, we do not know. Immunogenic responses are quite different for different diseases and their vaccines. For example, with pertussis vaccine, the booster will last for many years. With the flu, we are encouraged to get the vaccine every year. We do not know how long the antibodies for COVID-19 will last.

What happens if we get the first vaccine, but not the second – especially since there seems to be a shortage of the vaccines? The way the vaccine works is to have the first dose to prime your immune system. – get the body ready -- then the booster can target the protein spike. Your protection will not be as great as the 95% effectiveness estimate as promised.

Will people be negatively impacted as people cross state lines for vaccination? Each state was assigned vaccine inventory based on their population. Unfortunately, there have not been organized or consistent systems to deliver the vaccines. Most states that initially had no rules against interstate vaccinations have since made changes. In Georgia, you can go to any county to get your vaccines – but you must be a Georgia resident. Most issues have at the core, equity of distribution. Those who have the highest morbidity and mortality should have programs developed to reach them first. The sooner we get all people vaccinated, the better.

Patient Updates:

Gloria started on a clinical trial on January 5th – Dara and Velcade (sub-Q (subcutaneous). On her first round, she receives therapy twice weekly. Stay tuned.

Glenda was in remission 2016 – 2020, taking Revlimid. Since May, she has been on Dara (IV infusion). She went in every week for eight weeks and is now going in every other week for 8 weeks. Her CT scan showed very small holes in her spine. She is scheduled to have radiation to fuse the holes in her spine, which the doctor compares to holes in a kitchen sponge). She is hesitant and has tried to reach out to others who have had similar problems but will decide soon. She will do the chemotherapy first.

Emma has diabetes and thyroid issues. She has difficulties in taking REV. Her protein numbers are increasing. She got a bone marrow biopsy. She received a second opinion—was counseled to stay on REV to get her MM stabilized. She tolerates the side effects of REV – diarrhea, fatigue, no drive – just feeling sick. She is also doing physical therapy for back pain. One month ago, she felt left side pain – breast pain. She had EKG with her primary care doctor. She has lots of pain behind her breastbone. Both sisters have had breast cancer.

Carole is doing well. She pushes herself to be physically active each day – usually 5 miles/daily. She has animals, including 2 greyhound dogs who demand her activity; after almost a month, **Alma** has been moved from intensive care to a regular room at Emory. PLEASE keep all our members in your thoughts and prayers.

Announcements/Resources/Upcoming Meetings

- **COVID-19 Vaccines.** https://myvaccinegeorgia.com/ (includes Delta Aviation mass screening site; https://dph.georgia.gov/covid-vaccine (GA Dept of Public Health – includes Publix, Kroger, Walgreens, CVS, etc. across the state)
- New Patient Ambassador Program – Sanofi -**Sarclisa.** Deb Shafer – 816.756.5999
- **ASH in Review**. New drugs, CAR-T therapy, BCMA targeting therapies – Blenrep, Antibody Drug Conjugate (ADC). And your January Support Group Newsletter for Emory Winship updates and IMF for Dr. Durie's archived update.
- **IMF**. African American Initiative – Please join. Myeloma. org
- **MMRF 5K**. Will change format for fundraising event. Stay tuned.
- **Patient Power.** Exercise, even in small doses can improve bone density, balance, coordination, and stamina. Yoga, Pilates, Walking, and Swimming are recommended. Resistance training with bands better than weight training.
- **Patient Empowerment Network** (PEN). What are key factors in Myeloma Treatment Decisions?

- AMAZON Shopping? **Smile.amazon.com** – You can choose IMF, Atlanta Area MM SG, or a charity of your choice.

- Search for Clinical Trials: **SparkCures** – myelomacrowd.org, call IMF InfoLine for personal guidance 800-452-CURE (2873)

- Smart Patients. IMF

#Ask Dr. Durie. Should newly diagnosed high-risk smoldering myeloma be treated? Bottom line: It depends**.** With your doctor, monitor your myeloma. Be sure to discuss the following questions with your doctor**.** Do you have high-risk smoldering? And what would be a treatment option if there is an idea to move forward? And have a joint and careful plan with your doctor.

Patient Power. How long should one take **bisphosphonates** for Myeloma? Zometa, Aredia, or Xgeva (denosumab) – and what is the difference in them. For bone strengthening, generally for about 2 years, once per quarter in the second year. Kidney disease would be a factor in determining which to take. Xgeva is more expensive, so some insurance companies will not approve it. Be sure to maintain calcium and Vitamin D supplements.

New Drug Therapies, Precision Medicine, and More

- Selinexor (XPOVIO) – Karyopharm received FDA approved in December 2020 for first in class **with one prior therapy**. *Prior approval was for four prior therapies*. This oral medication in the class SINE (Selective Inhibitor Nuclear Transplant) is approved for once a week use with Velcade and dex.

- Precision medicine in myeloma. Dr. Gupta showed a chart of over **50 mutations** in MM – to underscore that everyone's myeloma is different. The MYDRUG (Myeloma – Developing Regimens Using Genomics) trials with MMRF along with the many drug trials are more targeted therapies.

- Emory Winship has COVID-19 vaccines available *for patients only.* They are also seeking to enroll those who get the vaccine into a study to monitor antibodies at four different intervals over the course of the year.

Respectfully submitted, Gail.