ATLANTA AREA MULTIPLE MYELOMA SUPPORT GROUP, INC.

Meeting Minutes
Northside Virtual MM Support Group
November 5, 2022

Business & News

Thank you to Nancy M for hosting the Northside November meeting with 40+ attendees. Dr. Ajay Nooka of Emory Winship Cancer Institute joined the Zoom session to update the group on the Emory WCI expansion, MMRF Cure Cloud research study and a deep dive in the Clinical Trials process.

Guest Speaker Presentation

Dr. Nooka informed us that the new Emory WCI building being constructed next to Emory Midtown Hospital will be completed within the next year. The present Winship Clinic has outgrown its space on the Clifton Road campus. It is very hard to get the rooms cleaned and ready between patient appointments, causing slowdowns and delays in the schedule. The new Midtown Clinic was designed with patient input and there will be a comprehensive myeloma treatment center on site. Nancy noted that the new facility is near the interstate which simplifies access for patients driving from remote locations outside of the city.

Dr. Nooka discussed the Multiple Myeloma Research Foundation (MMRF) research CureCloud that studies gene sequencing of myeloma particles found in the blood. There are currently 600 patients participating in the program. Active enrollment will be suspended on November 22, 2022, for 3-4 months to update study research and analysis. MMRF is looking for more patients prior to the November 22 deadline. The CureCloud study does not include patients in remission, so only patients with active disease should apply. Once registered, CureCloud will send a technician to your home to collect a blood sample for the study or you can contact Tom Prentice at Winship to arrange for an extra vial of blood at your next appointment. Active cancers release particles into the bloodstream and that is what CureCloud uses to sequence those cells. A report will be provided to your myeloma doctor along with a report to the patient. Dr. Nooka showed some physician report examples and the patient report. The patient report explains genes that are inherited and genes that are acquired over the course of a person's life as well as explaining mutation of genes. The goal is to link patients with certain gene mutations for which there are clinical trials. That is limited at this time. See the full information and register at www.mmrfcurecloud.org/patients Dr. Nooka said that this genetic testing is different from the FISH test done from bone marrow biopsy (BMB) when a patient is first diagnosed. The FISH test is looking for specific translocations of chromosomes that indicate high risk MM. The FISH test does not see other abnormalities because it is only looking for pre-determined gene sets.

Dr. Nooka continued with a presentation on the Clinical Trials process. In 2022, there were 1,908,030 new cases of cancer recorded in the US:34,470 were myeloma (1.8%) with 12,640 deaths from myeloma. Also, this year 1270 Georgians will be diagnosed with myeloma and 420 will die from MM. The goal is to dramatically reduce the number of deaths with new treatments that are proven effective through clinical trials. Dr. Nooka reviewed the IMWG criteria for myeloma diagnosis**. MGUS** is defined as: M-protein < g/dl; clonal plasma cells in BMB <10%; and no myeloma defining events *(CRAB)*. **Smoldering myeloma (SMM)** is defined as: M-protein ≥ 3 g/dl (serum) or ≥ 500 mg (24 hr. urine); Clonal plasma cells in BMB ≥10% - 60%; and no CRAB events. **Active myeloma**

(MM) is defined as: 1 or more CRAB features or Biomarker driven – 60% or more clonal plasma cells; serum FLC ratio ≥100; or >1 focal lesion detected by MRI. Clinical trials are being developed in all MM disease phases to try delaying patients from advancing to active myeloma with bone and organ damage. Clinical Trials have found that a few patients can fight MGUS by just altering the gut biome to improve the immune system's control of MM. Some clinical trials are actively treating MGUS and SMM to keep it from advancing. *Dr. Nooka stressed that a patient should ask about the purpose of a clinical trial they are considering. Also ask about the expected side effects.*

Dr. Nooka explained the phases of clinical trials.

- **Pilot trials** – newly developed clinical drugs are tested in rare and very aggressive diseases. Trials using these drugs are very limited in a research setting, but researchers do not know the drug's effectiveness vs the side effects to one's body.
- **Phase I** – This phase is to determine drug safety by testing a range of dosage levels. Phase I defines what the body does with the drug and what the drug side effects do to the body, in treating the disease. Phase I patients are monitored closely and are tested frequently during the early stages of treatment.
- **Phase IB** – This phase takes a new drug under clinical trial and adds an existing drug to see if better results can be achieved with a new combination therapy. Years ago, clinical researchers were happy to obtain positive responses in 10-15% of patients with a single drug agent, but that is no longer acceptable with the impressive results that so many drug combos are delivering. For example, Daratumumab (Dara) alone had 30% remission response while Bortezomib (Velcade) alone had 29% results, yet the drugs in combination have achieved a 70-80% response rate.
- **Phase II** – studies clinical drugs to determine its safety level. The clinical trial also evaluates effectiveness against the disease, generally based on *Progression Free Survival (PFS)*. PFS measures how long patients are on the treatment without their disease increasing to a new progression level. During this phase, side effects are identified and assigned a grade that classifies its intensity. Special focus on side effects severe enough that the patient needs medical interventions or stops treatment (Grade 3-4).
- **Phase III** – Compares the new treatment to the established *Standard of Care (SOC)*. At no time does a cancer patient receive a placebo which is unethical. The patients that do not get the new treatment plan receive the standard protocol. Note: SMM patients, observation without treatment is the standard of care.

Dr. Nooka then spoke about some significant clinical trials that Emory participated in. He discussed that Emory is gathering additional data within subgroup settings, such as: age, gender, race, co-morbidities. The information revealed that blacks had less benefit from certain protocols and these tests help to guide patient treatment decisions. He noted that at Emory, treatment median *Overall Survival (OS)* is 123 months which includes good quality of life. That is a very significant disease outcome compared to 20 years ago. The **GRIFFIN Trial** that Dr. Kaufman heads at Winship, *compared RVd vs. RVd+Dara* in frontline induction and maintenance treatment. This trial shows that response rates for CR (complete response) and better were greater for RVd+Dara at all timeline survival points, with the deepest responses after two years of maintenance: 82% vs, 61%. This was presented at ASH last year and may be updated later this year. These findings can also change the standard of care for newly diagnosed MM patients. Dr. Nooka also talked about a clinical trial headed by Dr. Boise with **Venetoclax** for *high-risk patients with t(11;14) abnormal chromosomes*. This trial is showing great response and Emory has the most patients on Venetoclax.

Dr. Nooka then talked about FDA approved **Teclistamab**, the first *T-cell Bispecific Engager Antibody* targeting BCMA and CD3. It is a 2-part drug where one-part attaches to BCMA on the MM

cell and the other part attaches to CD3 on a passing T-cell. This redirects the T-cell to the MM cell to destroy the myeloma cell. 165 patients participated in this trial with a median of five lines of therapy to a maximum of 14 lines of therapy. The *ORR (overall response rate)* of 63% represents a substantial benefit for these patients. Responses were durable and deepened over time. Side effects included fever and neurotoxicity, same as CAR-T. Dr. Nooka said that fever is a positive biomarker to treatment response. Watch for updates at ASH in December. Dr. Nooka reviewed the Winship team of doctors who see patients. He noted that 30% of patients in clinical trials at Emory are African Americans which exceeds national clinical trial participation which helps researchers to understand best treatment options for the subgroup.

Group Q & A

Q: A Patient has a good response to Pomalyst maintenance and asked if there were clinical trials for patients to go back to a previous treatment after a transplant. Does a transplant reset your immune system so that previous drugs can work again? **A:** The answer is unclear. For example, Revlimid kills off all MM cells that are sensitive to Rev, but it is unknown which MM clone cells cause progression. Patients can have numerous MM clone cells MM and different clone combinations are more active at different times. Your new immune system after transplant includes cells that have seen Rev already and may have now been resistant to the drug. Doctors do not know which combination will provide benefit after transplant and may find new drug combinations to work after relapse. **Q:** RVd therapy was successful in controlling MM for patients not eligible for transplant. After Rev maintenance, the MM is active again. Should Dara be added? **A:** Out of 100 patients, RVd plus Rev maintenance gave a median PFS response of six years. If disease progresses, do not use Rev again. *Try Dara + Kd or Dara + Pd.* (K=Kyprolis, P=Pomalyst). **Doris** commented that she had remission from Thalidomide and Revlimid. She is now on Pom/Ninlaro/dex and doing well. She likes the all-oral treatment without trips to the clinic for infusion or shots. **Q:** Patient is non-secretory. After Rev and Pom therapy, the MM returned. Treatment changes to Dara+ /Vel/dex and the pain is 99% gone. What is next? **A:** Get on a CAR-T waitlist but note that only four slots open per month. Maybe consider a bispecific. **Q:** Do any drugs complete Phase III after approval? **A:** Both Teclistamab and CAR-T were approved prior to completing Phase III which are continuing. Phase II shows benefit in relapse vs. standard care and benefit difference in earlier treatment before failing on four or more lines of therapy. CAR-T results for earlier usage in Phase III will be presented at ASH. In clinical trials, patients can "cross-over" if their MM progresses in the standard treatment arm, they can get CAR-T therapy. **Q:** Do patients have to change doctors to get on a clinical trial? **A:** There are 100's of clinical trials that centers can choose to participate in. Emory gets options to many trials but asks what benefit a trial is to their patients. Trials require that a specific site handles and reports everything for the trial – proper storage of drugs, monitored administration of treatment, evaluation of response, grading of side effects, etc. At Emory, all the clinicians are co-investigators, so patients do not need to change doctors within that clinic. If you see a trial that you want to join, appeal to your doctor to change sites to get it. **Q:** Once a patient is on a clinical trial, there is less contact with the physician. Is most of the treatment monitoring happening in the background? **A:** Every chief investigator knows the most about their patients. Your doctor is discussing your case at the clinical team meetings each week. Even if you do not regularly see the doctor, your labs are being closely monitored since your doctor is responsible for tracking your results. A clinical trial is an extensive network of communication and support.

Submitted by Nancy B.

Meeting Minutes
Southside Virtual MM Support Group
November 26, 2022

Business and News

Next Meeting: December 24, 2022 – **Christmas Eve – Patient/Caregiver Voices**. Join for an hour to share any updates – share a poem or a song – some grateful words for the New Year.

Group Discussion

Doris opened the meeting with a moment of silence and expressed many thanks, especially during this time of Thanksgiving, to all patients, caregivers, and supporters of the Southside Support Group over the past 16 years. There were over 30 people in attendance. **Ted A.** enthusiastically invited all men with myeloma to join the "For Men Only" Group on the fourth Tuesday each month at 6:00 PM. Ted says it is an energetic time of sharing experiences and talking about challenges and issues that are important to them, including the new patient portal at Emory, called MyChart. It is an energetic time when you can freely just chat with other men. We will post reminders of these meetings in advance via email.

Guest Presentation

The Southside group welcomed **Charise Gleason,** Advanced Practice Provider Chief and Nurse Practitioner from Emory Winship. Charise presented *Understanding Lab Values*, a topic requested by the "For Men's Only" group and the larger group as well. Understanding myeloma labs can be confusing, so as new members join the group presentations will be scheduled to support newly diagnosed patients and refresher slideshow for everyone. She delivered an excellent program and provided the PowerPoint attached to the group for reference.

Charise started the presentation with a quick review of what *myeloma is – an abnormal plasma cell*. The clinical workup diagnosis for myeloma includes the **CBC** (comprehensive blood count) – red blood count, white blood count, glucose, kidney function (creatinine), etc. along with serum protein electrophoresis **(SPEP)** and Urine Protein **Electrophoresis (UPEP)** About 30% of myeloma patients have light chain , as well as heavy chain in the urine while 15-20% of myeloma patients produce light chains only – *Kappa and lambda*. A bone marrow biopsy is conducted, along with image testing; PET scans and MRIs to help define your myeloma type and your health status. Labs defining and monitoring your myeloma status do change over time as your MM evolves.
In myeloma terms, **M- spike paraprotein** is the same as *M-protein*, or *myeloma protein*, or *monoclonal protein*. These are all different names for the same thing.

Serum creatinine can show a breakdown of muscle tissue which is filtered through the kidneys. The kidneys are remarkable organs and can function even at 10%. *Ibuprofen and NSAIDs (non-steroidal anti-inflammatory drugs) are hard on the kidneys and should not be taken by myeloma patients.* **Quantitative immunoglobulin** measures the amount of protein circulating in the blood. Most common are *IgG* and *IgA*. Less common are *IgD, IgE*, or *IgM*.

Classification of Myeloma include: (Please refer to the slides for more information)

- **Heavy chain** – 77% of patients – includes IgG, IgA (most common), IgD, IgE, or IgM
- **Light chain** – 20 % of patients will follow only kappa or lambda levels
- **Non-secretory** – 1-2% of cases have no detectable immunoglobulin.

Charise discussed **CRAB** criteria and the more recent **Slim CRAB** criteria as ways to diagnose and stage myeloma. CRAB refers to Calcium, Renal (kidney), Anemia, and Bone as indicators that more testing for myeloma is needed. The SLiM refers to the affected level of serum protein being greater than 60%, free Light Chain ratio of greater than 100, and any focal lesion as noted by MRI. Additionally, Charise talked about **cytogenetics** – more specific areas that might designate our myeloma as standard risk vs high risk. Treatment regimens are being developed to address very specific types of myelomas in the area of precision or personalized medicine. Sometimes there are translocated chromosomes (i.e.: (4;14) or t(11;14) or chromosomes that have been deleted (i.e.: 17p deletion).

Charise reviewed the research on a cure for myeloma and shared the slide of the tip of the iceberg seen above the water, with the greater portion of the iceberg below the water. There has been much progress achieving a state of Minimal Residual Disease **(MRD)** although it is not known how long that state can be maintained in different myeloma patients. There may be inactive or dormant myeloma cells lurking about for a relapse condition. While there is still much unknown, but certainly reason for hope. It is okay not to achieve MRD, and to have low levels of disease. Many patients continue to live long lives, never having gotten to MRD status. There are also many new drugs, drug classes, and combinations being researched and towards approval. The most important reminder in this myeloma journey is to openly communicate with your doctor/provider. Please share any changes in symptoms when they occur. Keep track of the symptoms for your own records as well.

Respectively submitted, Gail