ATLANTA AREA MULTIPLE MYELOMA SUPPORT GROUP, INC.

Meeting Minutes

Northside AAMM Support Group
January 8, 2022

Business & News:

Next Meeting: February 5 at 11AM.
Nancy will review the ASH updates and lead open discussion with patients and caregivers. The March meeting will be separated into Patients and Caregivers sessions for more specific discussions.

Annual Review of ASH Session:

We always look forward to the Annual review of ASH (American Society of Hematology) with the Winship team to begin the new year. The ASH Conference is where the latest research that impacts future treatment protocols in myeloma is presented. This year there were 879 abstracts addressing myeloma. Although there were not as many new treatments presented there were several long-term updates on existing treatments and clinical studies. This is meaningful as more patients are living longer and data on longevity matters to doctors and patients.

Dr. Sagar Lonial started the meeting with opening remarks of this year's ASH Conference that was held in Atlanta as a hybrid event allowing doctors world-wide to participate remotely. The myeloma research report included new data related to **MGUS** and **SMM** as well as long-term follow-up data on important MM clinical trials. Emory Winship has treated 2500 myeloma patients in the last year and is one of the top five MM centers in the US. Emory is at the forefront of testing several new myeloma drugs and the entire Winship team stands strong as they focus on improved outcomes in MM.

Charise Gleason spoke of the importance of the clinical trials at Winship. There are currently fifty-eight active trials in myeloma with thirty-seven still enrolling patients. Over one hundred patients were added to clinical trials in 2021. The clinical trials are supported by the dedicated MM doctors, pharmacists, nursing team, nutritionists, physical therapists, research scientists, and countless Winship supporting personnel.

Charise started with a review of clinical trial phases:

- **Phase I** – determine appropriate treatment for further evaluation.
    - small group 15-30 patients
    - Collect "Bench to bedside" data to find the safe dosing; decide how agent should be given; how the agent affects the human body; and evaluate pharmacokinetics.
    - One endpoint is DLT (dose limiting toxicity) to understand toxic effects related to the drug and protocol. This is typically assessed during the first cycle; accurate grading of toxicities is very important.

- Another endpoint is to determine MTD (maximum tolerated dose) which is the highest dose level at which $\leq 1/6$ of patients experience DLT.

- **Phase II** – determine whether an agent has activity against specific cancer type
  - large group < 100
  - Uses the dose determined to be safe in Phase I to test the effectiveness of the drug in a larger population.
  - Typically narrows the focus to people with diagnoses that are most likely to respond to therapy. Also assesses treatment for effectiveness as well as additional safety data.
- **Phase III** – determine treatment effectiveness compared to standard of care.
  - Trial may include 100s to 1000s of patients. Patients are randomized and trials are conducted at multiple institutions around the country.
  - No placebos are used unless standard care is not a treatment for that disease status.
- **Phase IV** – Post FDA approval to evaluate various goals.

Clinical Trial terms	
SD	Stable Disease
MR	Minimal Response
PR	Partial Response
VGPR	Very Good Partial Response
nCR	Near Complete Response
CR	Complete Response
sCR	Stringent Complete Response
MRD	Minimal Residual Disease
PR	Progressive Disease
ORR	Overall Response Rate
PFS	Progression Free Survival
OS	Overall Survival
DOR	Duration of Response
MTD	MTD Maximum tolerated dose
DLT	DLT (dose limiting toxicity)
RRMM	Relapsed Refractory Multiple Myeloma refractory is when treatment stops working
NDMM	Newly Diagnosed Multiple Myeloma
Median	the middle of the statistics where 50% were below that number and 50% above it
ADC	Antibody Drug Conjugates
CRS	Cytokine Release Syndrome

Dr. Nisha Joseph was the next speaker and reviewed the topics on the agenda:

- PROMISE study
- iSTOPMM study

- MGUS
- SMM – Smoldering Myeloma
- Iberdomide in RRMM/SMM trial

The **Promise Study** is funded by the *Stand Up to Cancer* campaign based at Mass General Brigham Hospital. The program is recruiting volunteer adults who are age 40 and above who self-identify as African American *and/or* have a close family member with myeloma. *Participants aged eighteen and older with two or more 1st and 2nd degree relatives are also eligible.* 7622 participants have been screened and divided by group into high-risk for MM or no high-risk features then subdivided by family history. Data has shown that the presence of MGUS increased by age from below 10% at age 50 to over 20% at age 75. The risk was higher in males and Black people.

iStopMM – **I**celand **S**creens, **T**reats, **or P**revents **M**ultiple **M**yeloma

Goals include evaluating the impact of screening for MGUS; integrate markers in risk for progression, evaluate the impact of screening on quality of life; create a biobank; and evaluate the effects of early detection and early treatment. From 2016 to 2018, all adult Icelanders were eligible to participate (148,708). 80,759 (54%) agreed to participate and 75,422 have since been sampled. They found 3725 with MGUS which include twenty-eight people with active MM. iStopMM randomized people with MGUS into three levels of follow-up. The group with more extensive work-up found higher incidence of disease. Bone marrow sampling was performed in 970 with MGUS, 105 (10.8%) were diagnosed with SMM. The prevalence of SMM in the total population was estimated to be 0.53% in people 40 years of ang or older. Although early detection and intervention is important, until results from this project are available, including data on survival and quality of life, they advise against systematic MGUS screening in healthy individuals.

Dr. Joseph next talked about **Iberdomide (IBER)**, developed as a next-generation IMiD, in the same class with Revlimid and Pomalyst. **IBER Phase I and II** was evaluated with different treatment combinations: alone, with Dex, with Dara + Dex, with Vel + Dex, and with Kyprolis + Dex. The patients in the study had a median of six lines of prior therapy with some up to fifteen lines of therapy and were refractory to three classes of therapy. Most side effects were in blood counts. These patients had a very low rate (<2%) of serious non-blood side effects such as fatigue, diarrhea, constipation, and rash. The results show a 26% patient ORR and the median PFS was 13 weeks. *Conclusion:* **IBER + Dex** demonstrated clinically meaningful and durable responses in patients with heavily pretreated RRMM (97% triple-class refractory), The treatment was well tolerated, and side effects managed with dose reductions and interruptions.

Dr. Jonathon Kaufman addressed the ***long-term follow-up (over ten years) of patients on RVd***. The median PFS is 65 months (5.4 years), and median OS is 126 months (10.5 years) for patients who started treatment ten years ago Next topic was an update on the **GRIFFIN** study after 24 months. This is the comparison of *Dara-RVd vs. RVd protocol* in transplant eligible NDMM. After transplant, the maintenance regimen is on DR or R for two years. Results showed that responses deepened over two years for both groups and MRD-negative rates improved throughout the DR maintenance period at double the rate of R group patients.

The **MASTER** trial looks at D-KRd induction, transplant, with no consolidation or maintenance if MRD negative is achieved. At 30 months, 91% of patients with 1 or 0 high risk genetics were progression-free. Overall survival in this group at 30 months was 96%. A German study of **Isa+RVd** (Isatuximab is Sarclisa) vs. RVd showed MRD-negative at the end of induction at 50%. Sarclisa is similar to Darzalex since both use the same target on the MM cells. Dr. Kaufman is also

involved with a **Phase I/II VenDd trial** of Venetoclax + Dara/dex vs. Dara + Vel/dex in patients with t(11;14) relapsed. The VenDd group achieved deep responses including MRD-negative.

Dr. Ajay Gupta talked about **Immunotherapy** in myeloma, which included an *overview of Immunology, CAR-T design, Bi-specific antibodies, and Antibody Drug Conjugates (ADC*). The goal of CAR-T and Bi-specific antibodies is to redirect T cells to attack myeloma cells using the part of an antibody that recognizes the myeloma. The **CAR T-cell therapy** collects T-cells from a specific patient and re-engineers the cells to recognize a target on myeloma cells and kill the cells. **Bi-specific antibodies** are not engineered to one patient but instead offer ("off the shelf") treatment to recognize two antigens – one on the myeloma and one on the T-cell. This directs the T-cell to the myeloma cell and activates the T-cell to kill the myeloma. There are different forms of bi-specific antibodies being developed. **ADCs** bind to the myeloma and bring along a cytotoxic drug. When the ADC is absorbed by the myeloma cell, it releases the drug that can cause cell death for the myeloma cell. There are other immune therapy drugs that are using newly identified targets on the myeloma cells.

Dr. Madhav Dhodapkar talked about CAR-T studies and then addressed COVID. The **CARTITUDE-1** study is in Phase 1b/2 using **Cilta-Cel** T-cell therapy. It is showing early, deep, and durable responses from a single infusion in heavily pretreated RRMM patients. Follow-up at 12.4 months has shown a manageable safety profile, ORR and sCR were 97% and 67% respectively. Overall, 12-month PFS and OS rates were 77% and 89% respectively. The rate of sCR was 67% at one year and rose to 83% at two years. At this time, the median duration or response has not yet been reached. MRD negative response was achieved in 92% of patients. PFS and OS was improved in patients with MRD negativity sustained for >6 and >12 months. **Cilta-cel** is currently under further investigation in patients with MM earlier in their journey, including newly diagnosed. These studies include outpatient administration.

The *FDA approved CAR-T therapy*, **ABECMA**, was in **KarMMA** clinical trials as bb2121. Dr. Dhodapkar reviewed the bb21217 trials for the same CAR molecule as bb2121 but is cultured to enrich T-cells to display more memory. The question is: *can these CAR-T cells persist and function for longer than the non-enriched CAR-T cells?* The results show known toxicities of CAR-T with low rates of CRS and neurotoxicity. In a selected group, ORR was 74% with 39% CR. The median DOR was 23.8 months for all patients, 34.8 months for patients with CR. The study has shown that the memory markers are associated with improved clinical outcomes. Dr. Dhodapkar summarized that there are high rates of response efficacy of several CAR-T therapies and new therapies against additional targets other than BCMA. However, more work needed to understand how/why patients relapse and how to prevent this.

Dr. Dhodapkar cited a large nationwide Veterans Affairs study on the **COVID** vaccine effectiveness in myeloma patients. It showed a higher percentage of breakthrough infections if myeloma treatment was within ~~the last~~ 90 days prior to vaccination: 5.2% vs. 2.6%. Also, there has been a higher percentage of breakthrough cases for those on Dara (9.1%). Further studies are needed to evaluate disease state, optimal type/timing of therapy, and to determine role of post-vaccination serologies and booster vaccinations.

Dr. Ajay Nooka spoke about **Bispecifics** and **Antibody Drug Conjugates** (ADC). He outlined the history of immune therapy in myeloma, starting with the approval of daratumumab (**Darzalex**) and elotuzumab (**Empliciti**) in late 2015 followed by Dara drug combinations in 2019. **Dara sub-Q**, Isatuximab (**Sarclisa**), and **Blenrep** (ADC) were approved in 2020 along with more drug

combinations in 2021. In the **DREAMM-2** study, Blenrep alone had a 31% response rate in highly pretreated MM patients, and it was found that meaningful responses were sustained despite dose modifications. Note that major *ide* effect is blurred vision that recovered after discontinuation of treatment. **DREAMM-5** trials are testing Blenrep in combinations and preliminary results show an ORR of 52%.

Teclistamab is an off-the-shelf, T-cell redirecting, bispecific antibody. It binds to *CD3* on T cells and can also bind to BCMA on myeloma cells to mediate T-cell activation and cause the destruction of the MM cells. The **MajesTEC-1 Trial** studied Teclistamab as a single agent and median follow-up at 7.8 months showed an ORR of 62%. Median time to response was 1.2 months which were durable and deepened over time. Additional bispecific antibody treatments are in Phase I trials, some with new targets on the MM cells other than BCMA. We will watch for future results on all these trials. Several of these have very good ORR and duration of responses.

As stated at the beginning, there is so much research happening in myeloma, and it is important to stay informed. To hear more on these studies, it is recommended that you review the slides and watch the video from Dr. Durie on the Best of ASH - Best of ASH 2021 Webinar (myeloma.org) The IMF has over 25 videos of researchers talking about their projects. You can click on any of these links to see a description of the research along with the conclusion before you watch the video. Click the following links to see the topics, many of which were discussed in the Emory ASH meeting –

- IMF Videos | International Myeloma Foundation – Click ASH tab for topics
- ASH 2021 Presentations- The Myeloma Crowd webinar review on January 22
- MMRF ASH 2021 Blog: ASH Day 1! - themmrf.org links to specific abstracts

As clinical trials and new treatments progress, the next update from researchers will be in June at these key meetings – American Society of Clinical Oncology (ASCO); International Myeloma Working Group (IMWG), and European Hematology Association (EHA).

Submitted by Nancy B

Meeting Minutes
Southside Virtual MM Support Group
January 22, 2022

Business & News

It is an exciting week of myeloma events. *Dinner with the Doc* -**Wendy Baer, MD.** Oncology Psychiatrist, Emory University, on Tuesday, February 22, 2022. *Patients and Caregiver Voices* **on** Saturday, February 26, 11AM. **–** *One Hour for Men Only.*

Guest Speaker

Tara S. Roy, MS, NP, AOCNP, Patient Advocacy Liaison of Takeda Pharmaceuticals was our speaker with the topic on ***Infection Risk: Importance of Vaccinations***. Tara started the presentation with a brief overview of myeloma and infection risks for myeloma patients.

Myeloma is a blood cancer. Blood is made up of platelets, red blood cells, and white blood cells that all perform different functions. Multiple myeloma develops in a subgroup of white blood cells called plasma cells which are found in the bone marrow that make antibodies to fight infections. When plasma cells become cancerous abnormal proteins are produced preventing the formation of normal blood cells and antibodies. Myeloma impairs the immune system. The risk for infection in myeloma patients is

much higher than a risk for someone without cancer. Treatments for myeloma suppress the immune system: *steroids* (**dexamethasone**)*, proteasome inhibitors* (**Velcade, Kyprolis**) *immunomodulatory drugs* (**Thalidomide, Revlimid, and Pomalyst/Pomalidomide**), and *high-dose chemo during* **ASCT**. Since age also weakens the system 22% of the myeloma population dies from infections. Infections are common complications in myeloma and a major cause of hospitalizations and deaths. Studies have shown that in countries where myeloma patients have received flu vaccines and pneumonia vaccination rates, death rates are lower. An observational study of 4,200 myeloma patients over 5 years and from 15 countries by Dr. Michael Thompson concluded that "the number-one cause of death in myeloma remains infection, and vaccines may prevent things like hospitalization, ICU, and severe consequences…". The vaccines included both live and killed vaccines… INSIGHT (April 2021) Tara provided a brief history on the importance of vaccines in the US starting in 1796 with the smallpox, and the development of rabies, diphtheria, typhoid, polio, and meningitis to present day COVID-19 vaccines. Prior to the COVID-19 vaccine, the quickest development of a vaccine for the mumps was in 1967 which took 4 years to develop.

Vaccinations

Vaccinations use your body's natural defenses to build resistance to specific infections and make your immune system stronger. Most vaccines are delivered by injection with some delivered orally. Live vaccines are not given to immunocompromised patients. Vaccines train your immune system to recognize *specific antigens* (dangerous germ, like virus or bacteria) to create *specific antibodies*.

The types of vaccines include:

Inactivated vaccines use the killed version of the germ that causes the disease. Inactivated vaccines may not provide as much protection as live vaccines, so several doses (booster shots) may be needed to provide ongoing immunity against diseases. Examples include hepatitis A, flu, polio, and rabies.

Live-attenuated vaccines uses a weakened (or attenuated) form of the germ that causes the disease. It creates a long-lasting immune response. Just 1-2 doses of most live vaccines give you a lifetime of protection against a germ and the disease it causes. Live-attenuated vaccines are NOT recommended for people with weakened immune systems, long-term health problems, or people who have had organ transplants. Live-attenuated vaccines protect against measles, mumps, rubella (MMR combined), rotavirus, smallpox, and yellow fever.

Messenger mRNA vaccines mRNA vaccines make proteins to trigger a response to the disease. mRNA vaccines are used for COVID-19.

Subunit, recombinant, polysaccharide, and conjugant vaccines use specific pieces of the germ, like its protein, sugar, or capsid (A casing around the germ) to respond to the disease. Used in hepatitis B, HPV, whooping cough, pneumococcal disease, meningococcal disease, and shingles.

Toxoid vaccines use a toxin (harmful product) made by the germ that causes a disease. Toxoid vaccines are used to protect against diphtheria and tetanus.

The Centers for Disease Control and Prevention (**CDC**) provide guidelines for who should get vaccines. Consult your doctor/healthcare team for recommendations. Special precautions should be observed with active current infections, like COVID. Other organizations with Vaccination guidelines include: **EMN** (European Myeloma Network); **IMF** (International Myeloma Foundation); **NCCN®** (National Comprehensive Cancer Network): **WHO** (World Health Foundation). CDC, EMN, WHO, and NCCN advise that myeloma patients receive **influenza vaccines** annually via injection (not a live vaccine) and scheduled re-vaccination during a time before or after interventions which compromise immunity. CDC, EMN, and NCCN recommend vaccinations against pneumonia with specifics depending on age and prior **pneumonia vaccinations.** The recommended **Zoster (shingles) vaccine** for patients is the Shingrix vaccine.

NCCN and CDC have no specific recommendations here. Shingrix is not a live vaccine, and two doses are recommended for optimal protection. For **COVID-19**, NCCN and IMF recommend vaccines by injections per labeling instructions. A Third COVID-19 shot is recommended for most cancer patients. Research indicates that response to the vaccine diminishes after 4 months and may be lower in myeloma patients.

FAQs for Vaccines

What is "Herd immunity?" This occurs when a significant proportion of the population becomes immune to an infectious disease, limiting further disease spread. It also protects those who are not able to be vaccinated, such as children.

Is there a link between vaccines and autism? 12 years after publishing a paper that turned tens of thousands against measles, mumps, and rubella (MMR) vaccines, the peer-reviewed *Lancet* journal retracted the paper. There is no known link between vaccines and autism.

Questions to ask your Healthcare Team about Vaccinations

- Should I be vaccinated for flu, pneumonia, shingles, and/or COVID-19?
- If yes, when should I get them?
- Who should provide them?
- What are the concerns with getting vaccinated?
- Should I get antibody testing after the COVID-19 vaccine? If so, how often?
- **Should I get my antibodies tested?** Antibody levels change over time. There is no protocol response to any one level that is considered a high level of antibodies. Talk with your healthcare provider about it and its usefulness for you.
- **What about vaccines after stem cell transplants?** Your body loses the immunity from all vaccines prior to transplant. Talk to your provider about when you will receive your vaccines again, including childhood immunizations.

General Business

We welcomed two new members to our meeting, **Antoinette**, and **Gwen** from Columbus. Many patients and caregivers shared news and updates on their care. **Carole O**. has found a dentist in Austell, Dr. Yadaz, who is knowledgeable about myeloma patients. We will share his specific information. **Gail** and **Lory** talked about Acyclovir (Zovirax) being replaced by Valacyclovir (Valtrex). They are antiviral drugs that work by interfering with viral DNA replication. Both drugs target the same viruses but valacyclovir provides longer duration of action, therefore, doses can be taken fewer times every day. Medicare may not cover the Valtrex. Please discuss with your doctor.

Gail asked the men in attendance if they thought it would be helpful to have a conversation just among themselves. After some discussion, the response was unanimous. Some discussion points included: *It is difficult to talk about health issues … hard to admit to weaknesses. This hit hard – it's one big challenge to talk about – feelings could be aggravated by COVID and the social isolation…my body, mind, and, and attitude have changed since my diagnosis"* … A men's only meeting will be scheduled.

Respectively submitted, Gail