January 2016 Northside Meeting- ASH Review

Nancy held a brief business meeting before the presentation. February meeting will be an open discussion to catch up with patient progress and hear from those who have changed therapy. March will be separate patient and caregiver sessions. March is also Myeloma Awareness Month and everyone is urged to think about where they could post a flyer about Myeloma. They can be posted on church bulletin boards, community centers, or local coffee shop. Molly suggested working with chiropractors or physical therapists to raise awareness since they are usually involved with patients who have bone pain that might be more than just a sprain.

Dr. Lonial opened the presentation noting that Emory now treats over 1600 patients with plasma cell disorders. In 2002, it was 150. There will be two new doctors joining Emory in July and one researcher who will start treating patients. The team will continue to work on reducing wait times in the clinic. He noted that all of the doctors practice with a common approach to make the best decision for the patient and maintain Hope for a good outcome.

Melanie Watson, RN OCN, gave the first presentation on Myeloma "Cliff Notes". This was a basic overview of MM to lay the foundation for the clinical information from the doctors. It helped a lot to get our brains started! Some of her points: MM is a cancer of the plasma cells; healthy plasma cells produce immunoglobulins (Ig) in response to foreign body invasion; MM cells produce abnormal immunoglobulin, which limits the body's ability to fight infections; about 65% of patients are IgG. Normally we have polyclonal Ig, with a broad pattern against numerous antigens. In Myeloma, we lose polyclonal Ig, and develop monoclonal Ig; this results in an 'M-spike' and infection complications. The symptoms are: bone pain, anemia, infections, and fatigue. The standard determination for active MM is the **CRAB** criteria – **C**alcium elevated (causes confusion), **R**enal complications (kidney issues), **A**nemia, and **B**one disease. The cause of MM is not known, but it is believed to come from chemical exposure.

Next speaker was Cathy Sharp, RN MN, Clinical Research Nurse, Team Lead. She showed how drug development can take 12 years or more to get from pre-clinical testing through clinical trials to FDA approval. She reviewed the phases of clinical trials. Phase 1 is to determine the safe dose, evaluate how the drug is absorbed and affects the human body. Phase 2 tests effectiveness in a larger population (<100) and further safety evaluations. Phase 3 enrolls more patients and compares the new drug to the standard of care usually in randomized trials at multiple institutions. At Emory, the targets for trials are newly diagnosed MM, smoldering MM, relapsed or refractory and trials are new drugs or new combinations. Emory MM has 36 studies with patients, 12 trials recruiting patients, and 20+ in the pipeline. The process to get on a clinical trial starts with your doctor to determine if this is the best option for you. Then you go through the screening process and informed consent. The benefits are that you will have access to the newest treatments before it is available to others and you will receive regular and careful monitoring. In addition, you are helping others by contributing to medical research. Important facts to know about clinical trials: participation is voluntary; your health and safety are always a priority; and you can stop treatment at any time. All of the eight new MM drugs and the standard of care drugs went through clinical trials at Emory. The whole team appreciates those patients who participate in clinical trials and make a difference for others. She listed over 35 people on the Emory MM Team.

Jonathan Kaufman said that ASH confirmed the treatment practices at Emory for the last eight years. Some of the studies reported at ASH were: Revlimid/Velcade/dex **(RVd)** vs. Revlimid/dex **(Rd),** early vs. delayed transplant, Cytoxin in combos, and new combos. The first step for new patients is to determine if they are a candidate for transplant. The goal of the first round of therapy is to get the deepest and quickest response possible to improve performance and quality of life as well as no impairment of stem cell harvest. In a study of RVd vs. Rd with continuous Rd maintenance, the results of partial response **(PR)** or better was 10% higher in RVd. Progression free survival **(PFS)** and overall survival **(OS)** were also more than 10% higher for RVd. In another study with RVd then transplant vs. RVd with no transplant with both groups followed by Rd maintenance, the results with transplant were higher than 10% improved response and PFS. The OS after four years in this study was similar for both groups, and only a couple of points higher for non-transplant patients. In a European study, comparing Cytoxin vs. Thalidomide in a triple drug treatment showed Thalidomide to be better. In the US, Revlimid has replaced Thalidomide and should show the same or better results over Cytoxin in a three drug treatment. Two other studies adding a HDAC inhibitor to RVd showed that both Vorinostat and Panobinostat had good results in these combos. Some of the clinical trials currently at Emory include: early vs. later transplant; RVd plus Elotuzumab, and Carfilzomib/Rev/dex plus Daratumumab.

Dr. Nooka spoke about relapsed MM. In evaluating four different studies; the odds for better results favored a three drug combo over a two drug therapy. In the randomized, double-blind TOURMALINE trial, Ixazomib/Rev/dex **(IRd)** vs. Rev/dex showed PFS of 20 months with IRd vs. 14 months with Rd, a 35% improvement. Similar results were obtained for high risk patients. The ELOQUENT-2 study compared Elotuzumab with Rev/dex vs. Rev/dex. The

results showed an improvement of PFS of 44% at three years and improved OS for the same period. Another study with Elotuzumab/Vel/dex vs. Vel/dex showed an improved PFS for both standard risk and high risk patients on the three drug combo vs. Vel/dex. A new drug, Filanesib combined with Carfilzomib, showed better results with the combination compared to Filanesib alone. A test of once per week Carfilzomib at a higher dose with dex showed a 77% response rate, which was better than the twice weekly lower dose. This study was to reduce impact on patients by going to a once per week IV of Carfilzomib. In a study with a new proteasome inhibitor, Oprozomib, with Pomalidomide and dex, all patients except one showed control of the disease. Dr. Nooka said that the key to gaining long-term survival is the availability of new and effective anti-myeloma therapies. Bottom line: there are more drugs coming and new combinations are showing good results.

The last presentation was from Dr. Lonial on Immune Therapy. He described three types of immune therapy. Passive immunity targets a single receptor and is a truly "targeted therapy" like the monoclonal antibodies. Adjuvant therapy is an immune booster. Adjuvants may be added to a vaccine to enhance the efficacy of a vaccine by helping to modify the immune response. Active therapy delivers cells as done in an allo transplant or Car T-cells. This has a higher risk of side effects on other targets in the body. There are multiple targets for monoclonal antibodies (MoAB). It is great news that Elotuzumab **(Elo)** and Daratumumab **(Dara)** have been approved by the FDA, but that is only two targets. Dr. Lonial showed a chart with nine other MoABs in development and four in preclinical activity. CD-38 is expressed on Myeloma cells and Dara binds to CD-38 to induce cell death. In a Phase 2 study of Dara as a single agent, in patients with three or more prior therapies, the response rate was 29% with one year survival rate of 69%. With Rev/dex added, the response rate increased to 81%. Dara and Pom response was 71% while Pom alone was 30%. The Imids (Rev, Pom) with MoAB is a great combination. In other research, the PD-1 pathway is often exploited by tumors to evade immune surveillance, so the immune system cannot destroy the tumors. Pembrolizumab **(Pem)** blocks this receptor and reinvigorates the immune system, allowing it to target and destroy cancer cells. Pem, combined with Pom and dex, had a reduction of M-spike or free light in 94% of patients, with the majority having more than 50% reduction. Research on Car-T cells is showing promise and more results will be available at ASCO in June and ASH next year. New MoAB targets can help overcome clinical challenges. How to target multiple receptors in a single agent remains an open question. So much more coming. Stay tuned!

Questions and Answers

FDA Approval of New Drugs:

Q: We have heard several different terms about how some recent myeloma drugs have gone through the FDA review process. How do the "fast track" and "accelerated approval" designations affect the timeline for FDA approval?

A: If a new therapy has the Fast Track designation, data on that therapy can be submitted to the FDA as it becomes available rather than waiting for all of the data to be submitted together. This speeds up the review process. The Accelerated Approval designation allows a new therapy to be approved before a phase 3 study has been completed and the FDA must respond within six months. The phase 3 trial must still be completed for the therapy to receive final approval.

Q: What is a phase 3 trial? Could patients receive a placebo?

A: The purpose of a phase 3 trial is to compare a new treatment approach against a current standard of care. These trials help identify the best treatment for a given treatment setting. Without phase 3 trial data, we do not know which approach gives the best balance of efficacy (how well it works) and toxicity (side effects). Patients on cancer trials do not receive placebo; everyone receives at least the current standard therapy.

Newly Approved Therapies:

Q: With so many new drugs approved, which is the best to use?

A: A single optimal therapy has not been identified. Several factors are considered when selecting the right therapy for each person, including clinical trial evidence, biological characteristics of that person's myeloma, their prior treatment history, and **patient preference**. (Note that this requires that patients be up-to-date on treatment options.) The advantages and disadvantages of each option are then weighed to make a decision. A commonly used newer regimen for early relapse (1-3 prior treatments) is Pomalidomide plus a monoclonal antibody. Two monoclonal antibodies are newly approved: Daratumumab (Darzalex) and Elotuzumab (Empliciti).

Q: Can the new drugs be used in any patient with relapsed or refractory myeloma?

A: Each drug has a specific indication for its use, specifying how many prior therapies patients must have had and, in some cases, what types of therapies. These indications can change as new clinical trial data become available.

Q: Are the new antibodies being used for the initial treatment of myeloma?

A: Not yet in clinical practice—only in clinical trials. Randomized trials are needed to determine the best approach for the initial treatment of myeloma. These trials are enrolling only patients who have not yet started treatment.

Q: What are the adverse effects of Daratumumab?

A: A primary risk is the potential for developing infusion-related reactions that occur when the therapy is being infused. These reactions, which occur in about half of patients, can cause fever, chills, nausea, and other effects. These medications are administered in the hospital so infusion reactions can be addressed promptly. The risk is greatest in the first 1-2 doses. It is important to keep a journal on the first infusion (and all infusions) and note timing and intensity of side effects so they can be addressed by the team at the next visit.
Q: How is single-agent Ixazomib used?
A: In instances where single-agent Velcade had been used, Ixazomib can now be used.
Stem Cell Transplants:
Q: What is the role of autologous stem cell transplant **(ASCT)** in relapse?
A: This was not presented at ASH 2015, but other data suggest that a second transplant is an option. It depends on the duration of remission after the first transplant, cytogenetic factors, and a person's general health. The first step would be to get back into remission then undergo the transplant.
Q: Have any of the recent trials shown that we can bypass ASCT?
A: ASCT still appears to give the longest duration of first remission so it is best to use ASCT when possible. However, some trials have enrolled patients who have not undergone ASCT and they have shown long survival.
Q: Is there any role for allogeneic transplant?
A: Allogeneic transplant (using donor cells from another individual) has been studied for 30 years, with some studies showing a benefit and others showing no benefit. It is a very high-risk procedure and is generally not recommended outside a clinical trial.
General Questions
Q: How is relapse defined?
A: The International Myeloma Working Group has developed criteria for relapse; often relapse is detected by an increase in the M-spike. However, an increase in the M-spike does not necessarily mean that treatment must be restarted immediately.
Q: When is a response to a new therapy assessed?
A: After the first month; responses often occur early.
Q: How does the subtype of myeloma (IgG, IgA, etc, and kappa/lambda) relate to the disease risk?
A: These factors do not affect disease risk—they are a way to follow the disease. However, IgA may be associated with higher-risk disease because more patients have the 4;14 translocation that confers higher risk.
Q: How is smoldering myeloma being treated?
A: Clinical trials are underway to determine the best approach. The standard of care today is observation.
Q: What is the role of minimal residual disease (MRD) in planning treatment?
A: This is still being evaluated. MRD may be a useful prognostic marker but it is still being studied in clinical trials.
Q: Are we heading towards a cure for myeloma?
A: A subset of patients have already attained a "cure", with long-term remissions, today. To increase the number of patients getting to this point, it will be important to look at differences between different patients to better understand the biology of multiple myeloma. A combination of understanding the underlying biology and identifying important mutations will help find the weaknesses of myeloma cells that are left after induction therapy. Dr. Lonial said "The Myeloma cells left after a transplant are the one that will cause trouble down the road." Targeting these cells will be important to reducing the likelihood of relapse.

Submitted by Nancy and Mindy

Southside Multiple Myeloma Support Group
January 2016

The January 2016 meeting of the Southside Atlanta MM Support Group was cancelled due to icy conditions. The topic of discussion was to be Living Longer with Multiple Myeloma. This is an important topic as new treatments are approved and patients can expect to live much longer than in years past. This discussion will be held at the Southside meeting on Feb 27, along with review of the new treatments.

Summary of MM Action Month
As you know, March is **Myeloma Action Month**. IMF has changed the name from Myeloma Awareness Month to reflect educational and outreach activities that will be conducted to increase awareness in the community. Action will

lead to even more awareness. To achieve this objective, the following activities are being planned. Special thanks to Doris, Alma, Vermell, Paulette and especially Gail for the hard work planning and coordinating activities to develop strategies for this year's Myeloma Action Month.

Myeloma Television Interview: Lynn Vaughn, veteran CNN news anchor and **current** host of Fulton Government TV "HealthLine", will interview **Kimberly, Sandy and Nancy.** The interview will focus on the disproportionate impact the Myeloma in the African American community, importance of regular annual visits to your primary physician and the importance of early detection. "African Americans are at higher risk for myeloma yet respond better to treatment, **early diagnosis is the key**." Dr.Durie. The Myeloma segment will be aired during the month of March on Fulton Government TV on **Comcast Channel 21** in the county and on **U-verse on channel 99** in the region. Also, it will be found on **Youtube** once it is aired.

Concerned Black Clergy: On March 7th Vermell, and Tricia (LLS) will present information about Myeloma to representatives of the Concerned Black Clergy (CBC) of Metro Atlanta. The message of early detection will be stressed and desire to connect with "ministers of health" from each congregation. (It is our hope to work with the "ministers of health" in churches, Synagogues, Shuls, Temples, and Masjids, to inform them of Myeloma and the importance of early detection). CBC is the primary, proactive and principle-centered organization comprising more than 75 mostly of African-American ministers and leaders of faith communities. Their mission is to provide leadership, advocacy and service to the homeless, helpless and hopeless in our community. Also, to provide support, Doris, Gail, Nancy, Paulette, Alma and Nancy will be in attendance. Vermell was honored by this group last year and has visited the meetings several times. At least two of their members passed away from Myeloma within the last few years; they were also members of our Myeloma support group.

Radio Interview: On March 8th Gail and Vermell will participate in an interview on WYZE Radio station 1380 AM. The radio show is an hour long and will allow listeners to call-in with questions. This is the third time our Support Group has participated in Myeloma Month Interviews

Church Bulletins: Seven members agreed to work with their churches to have a short paragraph placed in church announcements/bulletins about Myeloma.

Finally, all members agreed to start giving out the Atlanta Area MM support group brochures in clinics and doctor offices and wear buttons that "Ask me about Myeloma"

Below are talking points to be shared during each of the above activities. Alma developed these talking points.

Talking Points on Multiple Myeloma

Important message: Experts have brought up Myeloma in Blacks previously, but this year, there is more specific focus on why and how blacks are impacted.

- Multiple myeloma (or myeloma), is the second most common blood cancer (after leukemia) worldwide, is a cancer of plasma cells in the bone marrow. It is called "multiple" because the cancer can occur at multiple sites.
- Multiple myeloma currently affects more than 100,000 people in the US, with an estimated 20,000 new cases diagnosed each year and 10,000 losing their battle each year.
- Once a disease of the elderly, myeloma is increasing in people under 65. It is becoming more common in younger patients with possible links to environmental toxins.
- Myeloma affects African Americans at twice the rate of Caucasians. There is an increased risk of MGUS (monoclonal gammopathy of undetermined significance) in African Americans. MGUS is the precursor to myeloma. African Americans can do better with earlier diagnosis and treatment – with full access to novel therapies. This transition from MGUS to myeloma occurs in African Americans same as other populations. But African Americans are more likely to develop MGUS, which raises the probability of Myeloma.
- Some common symptoms are bone pain, anemia, kidney issues, frequent infection and extreme fatigue
- Because myeloma is a relatively rare disease, there can be a delayed diagnosis, leading to delayed treatment. For this reason an increased awareness of myeloma for clinicians and the general public will lead to earlier diagnosis allowing people to live longer.
- Although the causes of multiple myeloma are uncertain, certain professions have a higher risk factor. Exposure to pesticides, nuclear radiation, and petrochemicals are considered to be important trigger factors. There is a higher incidence of myeloma among workers at the 9/11 site.
- Although there is no known cure for multiple myeloma, patients are living longer with this disease due to improved treatment and early detection. The quality of life is much better. There are many more drugs (and more targeted drugs) to choose from to control the disease.
- Caregivers play a tremendous role in the well-being of patients. But stress and fear can take a toll on caregivers.
- We are fortunate to have three Support Groups locally. Support Groups help us to stay informed; we can share experiences, and learn more effective skills in communicating with providers. We can learn a lot about access to care –

for financial support, for paying for drugs, and other services needed by myeloma patients. (Support Groups: Northside, Southside, and Emory Winship Cancer Institute)

- Early diagnosis is key to better outcomes with myeloma. Annual tests with primary care providers are important to tracking any changes in tests. But we must be accountable as patients and families. We are our own best advocates. Find out what numbers are important to your provider – what is your goal blood pressure, blood sugar level, white blood count, red blood count, etc.
- Increased funding for multiple myeloma research, education and awareness programs is essential in the diagnosis, treatment, and quality of care for patients.
- The need to raise awareness for this often misdiagnosed disease led the IMF to establish March as Myeloma Action Month.

- Thank you for giving our support groups the opportunity to increase awareness locally of multiple myeloma.

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