November 2017

Northside Multiple Myeloma Support Group Meeting
November 5, 2017

Business

There are no more financial support funds available from the LLS as reported from our members who use them. Most of the resources for financial assistance to MM patients no longer have funds available. Patients are urged to contact the pharmaceutical manufacturers. See the references in the Southside notes, below.

The IMF Living Well webinar on How to Talk to Your Healthcare Team was on November 9 and the replay is available on the IMF web site. Also available is the prior webinar on Making Sense of Tests and Results. For access to both replays – https://www.myeloma.org/understanding/imf-tv/living-well-myeloma of go to Myeloma.org or go to Myeloma.org, click on Education at the top of the page then select IMF TV and choose Living Well with Myeloma.

One new member, Jeff was diagnosed one year ago and had a transplant in April at Emory. He is now in remission.

The group broke into separate discussion rooms for patients and caregivers. Jim Mahoney led the patient group and Ed Steinman facilitated the caregivers meeting.

Patients Meeting:

Discussion on disease onset and current treatments within the group. Lactose intolerance was mentioned as a side effect with taking Revlimid. Drug side effects are a balancing act with food and secondary medications which are needed to help with the symptoms. Severe cases of side effects are interrupting normal life. Patients end up being home bound; not eating; and dropping certain foods out of their diet. Ask your physician about Colestipol (Colestid), which a few of our members are taking to help control the diarrhea. Lory M. wanted patients to know about using Colestipol to help with diarrhea side effects of Revlimid. Welchol, which was discussed at the last meeting, works about the same but isn't usually covered by insurance and Colestipol is covered. Also, although the prescription calls for taking 2 tabs twice daily, she finds that 1 tab once a day works and feels it's better to start on lower dose and work up if necessary. She has no side effects and takes it every day.
The patient group discussed foods in our diet to add and subtract based on how we react. Request help from your physician and healthcare team. A number of patients are using a variety of both old and new drugs. Cramps in legs – pickle juice/Club soda (ensure it has quinine), exercise/stretching.

One patient in the group took a quick count of years of experience with the disease – 148 years of Myeloma experience was in the room. We felt this was pretty impressive and speaks about our knowledge of the disease and the drugs we are all using today.

Everyone pitched in to clean up!
Submitted by Jim M.

Southside Multiple Myeloma Support Group Meeting
Saturday, November 25, 2017

Doris opened the meeting with asking all to take a moment of silence. There were 20 present. We were happy to meet members of **Pat C's** family who were visiting from California, Ohio, and Washington. Bert, her sister that we have heard lots about was present. We also recognized Pat for the work she and her church members have done to raise money for IMF – and for the generous donation from her church again this month. **Next Month: Focus on Members/ Open Discussion**

Guest Speaker: Leon Bernal-Mizrachi, MD; Emory/Grady Myeloma Specialist
The Bernal-Mizrachi laboratory at Grady specializes in studying cancers of the immune system such as lymphomas or myelomas. Based on the premise that the cancer of each patient has unique characteristics, Dr. Bernal-Mizrachi's lab is focused on creating new technologies that allow matching each patient's unique cancer growth signals with specific therapies that can block their cancer signal growth effect. Their studies have provided new genetic indicators that could guide doctors to select the best combination of therapies for each patient. Ultimately, Dr. Bernal-Mizrachi's passion is to improve the outcome and reduce the toxicity of the therapies used to treat lymphomas and myelomas.
Please take note of much new vocabulary from this presentation. IMF has a publication that will go into further detail to help us understand better any terms that are confusing for us (IMF – Myeloma Terms and Definitions). The link is in the Sources section of this document.

Myeloma and Immunotherapy
Immunotherapy is the newest approach to multiple myeloma treatment. It is an umbrella term that describes different ways to stimulate the **immune system** and enhance its ability to attack cancer cells. Many of these treatments involve antibodies that target specific proteins found on multiple myeloma cells.
One class of drugs is referred to as **Monoclonal Antibodies**. Monoclonal antibodies (**mAb** or **moAb**) are antibodies that are made by identical immune cells that are all clones of a unique parent cell. There are two drugs in this class – Daratumamab (Darzalex) and Elotumumab (Empliciti). ***Antibodies****, also called immunoglobulins, are proteins manufactured by the body that help fight against foreign substances called* ***antigens****. When an* ***antigen*** *enters the body, it stimulates the immune system to produce* ***antibodies*** *(The immune system is the body's natural defense system).*
The immune system recognizes cancer as a normal part of the body, not the enemy, even

though cancer is made up of abnormal cells. Researchers are finding the key to help the immune system identify cancer as abnormal and destroy it. A healthy immune system should take care of cancer in normal conditions. Myeloma cells are sneaky, and have learned how to hide from the immune system and produce a false "friend signal" so the immune system does not attack it. Elotuzumab stimulates the internal systems to kill the myeloma cells. It targets the protein SLAMF7 (**s**ignaling **l**ymphocytic **a**ctivation **m**olecule F7), a protein found on myeloma cells in more than 95 percent of people with multiple myeloma, making it an excellent target for treatment. Daratumumab creates holes in the cell membrane that causes it to die. It also blocks the "friend" signals so the immune system will attack it. Darzalex attacks the antigen CD38.
Cancer is imperfect but its adaptability allows it to survive. How does immune therapy work? The newer drugs specifically attack myeloma cells, where older treatment also destroyed many healthy cells. The antibody is like a glove – and the myeloma = "the ball." When the glove catches the ball, it uses multiple ways to destroy it (the MM cell). It's like a triple threat – it ruptures the membrane of the cell, attacks the cell, and targets the signaling pathways of the MM cells. *An **antigen** is any substance that causes your immune system to produce antibodies against it. This means your immune system does not recognize the substance, and is trying to fight it off. An antigen may be a substance from the environment, such as chemicals, bacteria, viruses, or pollen. An antigen may also form inside the body (Medline, National Library of Medicine, NIH).* Currently, the monoclonal antibodies are used in relapsed or refractory myeloma.

Another immune therapy in development is **CAR-T therapy** (**C**himeric **A**ntigen **R**eceptor). This therapy uses a patient's own immune system cells. After collecting blood from the patient, T cells—the primary killing cells of the immune system—are separated out and engineered to express a special type of receptor, a chimeric antigen receptor, or CAR.
A less familiar immune therapy is called **Checkpoint Inhibitors.** Checkpoint inhibitors are monoclonal antibodies that target proteins found on the immune system's T cells. T cells are important in eliminating cancer cells and virus-infected cells. There are a number of proteins on T cells that serve as "checkpoints," allowing the cells to be turned on and off as needed. Checkpoint inhibitors work by either blocking molecules that inhibit T cell activity or by activating those that stimulate a response. In these two ways, checkpoint inhibitors "take the brakes off the immune system," harnessing its full power to attack cancer cells. Several clinical trials are being conducted using Keytruda® (pembrolizumab) for MM. Keytruda is directed against the PD-L1 (**p**rogrammed **d**eath **l**igand **1**) marker and is already approved for use certain patients with melanoma or lung cancer (MMRF). **Vaccines** work by stimulating an immune response against tumor-specific antigens, or substances that the body considers foreign. Several vaccines are being evaluated in clinical trials in myeloma. For example, one vaccine is being tested in patients already on an IMiD who are near remission to see if this added treatment improves outcomes.

Researchers continue to seek drugs and mechanisms that kill the myeloma. All organisms must adapt to survive and the same is true for myeloma. Launching many different attacks against myeloma reduces the adaption. The new drugs work well in relapse and it is important to get a

deeper response to reduce the adaptability of the cancer. Once the cancer adapts, it is harder to treat. The latest concept is to identify patients with high-risk smoldering myeloma and treat it early. The protein levels, free lite ratio, and genetic abnormalities define it as high risk. These patients have a higher risk of progressing to myeloma and should start treatment before too much damage occurs.
Patients should consider all aspects of a regimen when deciding about treatment, For example, Velcade is a subcutaneous injection. Daratumamab is a 5-hour infusion. Research is ongoing to make Darzalex delivery also subcutaneous.

Dr. Bernal then talked about some important **clinical trials**. He reminded us of the definitions of and differences between Phase 1, Phase 2, and Phase 3 clinical trials. In Phase 1, the researcher is trying to determine what dosages are tolerated best by patients, what are the side effects, and if the drug is safe. Phase 2 helps determine how many people respond to the treatment and Phase 3 studies, where there may be hundreds of participants; the goal is to determine if this drug is better than the current 'standard of care.'
One trial is called ELOQUENT, with Dr. Lonial as principal investigator. It is comparing Revlimid with Dex (Rev/dex) to Elotuzumab with Revlimid and Dex (Elo/Rev/Dex). After three years, the progression free survival (PFS) was 28% for Elo/Rev/dex compared to 18% for Rev/dex alone. Also important, the overall survival (OS) after three years was 43% for Elo/Rev/dex versus 39% for Rev/dex. Most of the side effects of the Elo/Rev/dex were infusion reactions and cough in 70% of the patients, but most were only on the first dose.
Dr. Bernal said that all medications cause side effects. Aspirin can cause ulcers, a multi-vitamin can cause stomach problems, and even food can cause problems from too much salt, sugar or fat! The new antibodies fire up the immune system to attack the cancer, as it should do. Clinical trials combining Elotuzumab with Velcade showed less benefit. A main side effect in that trial was reaction to the infusion. Daratumumab attacks the myeloma in multiple ways. It also alerts the immune system to attack the myeloma, but it also causes cell death through multiple methods on the surface of the cell.
Dr. Bernal talked about another clinical trial using Daratumumab with Revlimid and Dex (Dara/Rev/dex) compared to Revlimid and Dex (Rev/dex) alone. The results showed Dara/Rev/dex had very good partial response (VGPR) or better in 76% of the patients while Rev/dex was only 44%. Complete remission was 43% for Dara/Rev/dex and 19% for Rev/dex. Another trial showed one year PFS of 60% for Dara with Velcade and dex versus 27% PFS for just Velcade and dex. All these **studies reinforce the recommendation to use three drugs to treat (triplet) versus two drugs (doublet).**
Grady Hospital is now recruiting for a clinical trial (n=510), called the PINR Trial, for personalized treatment. This trial is using genes to predict response to a proteasome inhibitor, Ninlaro. This trial is divided into two groups based on certain genetics. The trial, based at Grady, is to understand the difference of race on treatment outcomes. More African Americans have the genetic abnormality for this trial. The Grady MM clinics seek to match the cancer with the drug therapy, which should result in less toxicity and lower treatment costs. This trial will also take place at four other centers. If you are trying to decide about your next course of treatment, please contact Dr. Bernal for more details and whether you are eligible for the trial.

Knowledge Gained through Research

We are still far from knowing what causes Multiple Myeloma. Over time, we have learned that MM needs to be treated forever – maintenance is necessary. If you take someone off maintenance, they are likely to have a shorter remission period. Myeloma is becoming more of a chronic disease (like diabetes) versus an acute health issue. Survival from MM after 10 years of diagnosis is about 80%. About 12 years ago, survival of 2-3years after diagnosis was more common.

We know that MM occurs 2-3 times as often in African Americans as in Caucasians. Compared to whites, blacks have a lower risk from MM. Whites seem to respond better to proteasome inhibitors (Velcade, Carfilzomib, and Ninlaro). More African Americans have an NFKB2 genetic abnormality or damage. At Grady, they have found that 50% of MM patients have this abnormality –10% of patients at the Mayo Clinic (Rochester, MN) have the abnormality. Studies of racial disparities in MM are being conducted among patients at the Veteran's Administration. The MM team at Emory meets every week to review myeloma patient cases. They discuss remission of patients of high, intermediate, and low risk patients and how to improve the patient experience.

Dr. Bernal's Q & A:

Q – Is a transplant still needed? A – As of now, the transplant is still winning. Unfortunately, many who would do well with a transplant are not getting it. We must do better education. A transplant may not be needed in ten years. At Grady, the overall survival rate from transplant is 80% at ten years. African Americans do better with Revlimid and transplant while Caucasians do better with Velcade. Using the same treatment standard, Grady has better outcomes than Emory.

Q – Is dex needed for maintenance? A – As people age, their metabolism changes. A younger person may get 20 mg dex while an older person may only get 10mg or none. Diabetes is also a factor in dex dosage.

Q – Is there an age limit for transplant? A – The age limit for Medicare is 75, but elderly need less toxic treatment.

Dr. Bernal noted that Grady has 400 myeloma patients and it is increasing.

Announcements/Resources/Upcoming Meetings

• Financial Support for MM treatment. – As of November 16th, LLS had co-pay assistance available. It appears to come and go. They are closed for the Thanksgiving Holiday and will open on Monday, November 27 @ 8:30 A.M. Contact hem at copay@lls.org or call 877.577.2672

• ASH Satellite Symposium. Online Webinar. Getting Clear Answers to Complex Treatment Challenges. Case Discussions. 12:30 PM - Marriott Marquis. FREE
https://www.myeloma.org/videos/getting-clear-answers-complex-treatment-challenges-multiple-myeloma-case-discussions

• IMF – Received a 4- Star rating from Charity Navigator. The rating is based on Financial Health and transparency.

• Ask Dr. Durie. "What may be causing heart and kidney issues in an elderly patient with no bone lesions."

• Going Shopping at Amazon? Use this address and make an easy, painless donation to

IMF. www.amazon.myeloma.org . More Fundraising, Jameca Barrett is selling Holiday Gift Boxes of Dexter Myers Cookies. A Deluxe Box of 40 cookies is $50. Proceeds benefit IMF

• Veterans and Myeloma Legislation. The Advocacy Team at IMF continues to track and support legislation -- now especially for Vietnam Veterans who were exposed to Agent Orange. This team is also working to keep the costs of cancer care down Watch your e-mails for ways you can help.

• Searching for Clinical Trials. Myeloma Matrix 2.0 Smart Search makes it much easier. - Myeloma.org/matrix

From Myeloma Today

Darzalex (Generic Daratumumab): Soared through FDA approval in relapsed and refractory MM as a single agent combined with Revlimid and Dex, Velcade and Dex, and Pomalyst and Dex. This is the first approved monoclonal antibody.

Xgera (generic Denosumab) is a monoclonal antibody approved for the prevention of skeletal event (bone damage) on patients with solid tumors (not blood cancers like leukemia, lymphoma, and myeloma). With the largest number of participants ever in a myeloma study (N=1,718), Xerga performed as well as Zometa (a bisphosphonate therapy). It had significantly lower rate for kidney side effects. Amgen has submitted application to FDA.

Financing MM Treatment

Check regularly: https://www.myeloma.org/article/co-pay-assistance-programs-update Patients are also advised to contact the financial aid programs of the drug manufacturers directly. The status of funds seems to change on a regular basis. Do not hesitate to revisit often.

Celgene's (Thalomid, Revlimid, & Pamalyst) patient support web portal: https://www.celgenepatientsupport.com/

T**akeda Financial Aid**: Ninlaro 1Point Program: https://www.ninlaro.com/cost

Velcade Support: http://www.velcade.com/paying-for-treatment/

Amgen Kyprolis: Amgen Assist 360 Program: http://www.amgenassist360.com/patient/kyprolis-cost-nurse-ambassadorassistance/

Janssen CarePath Program: https://www.darzalexhcp.com/cost-support/janssen-carepath#affordability

Sources:

1. **National Library of Medicine -** https://medlineplus.gov/ency/article/002224.htm
2. **MMRF -** https://www.themmrf.org/multiple-myeloma-knowledge-center/myeloma-drugs-guide/drug-classifications/immunotherapies-and-antibodies/
3. **IMF -**https://www.myeloma.org/sites/default/files/images/publications/tools/glossary.pdf

Respectfully submitted by Nancy, Paulette, and Gail.