Northside Meeting Notes – January, 2015

The January meeting was held at the Emory Winship Cancer Institute conference room. Winship doctors presented a summary of the information from the December 2014 meeting of ASH (American Society of Hematology) and how clinical trial results will impact patient treatment.

Nancy Bruno held a brief meeting before the presentation began. The group was glad to see **Hector** after his recovery from pneumonia. He said that he appreciated all the prayers and support. **Gail** spoke about her experiences at ASH. She said that there was a lot of information about clinical trial results. Gail noted that every presenter of clinical trial results thanked the participating patients and their families first. The research cannot move forward without the contributions from the patients. **Georgia** is a new patient who was diagnosed in June 2013 and wants to learn more about her options. **Suzie** had a transplant in 2009. When she was diagnosed in January 2009, she expected to live only 2-3 years and is happy to report that she is still around. Her MM returned in June 2014 and she went on Revlimid maintenance. She had a bad reaction to Revlimid with mental issues and felt "demented". Suzie is now on Velcade and dex as maintenance. **Beth** had a transplant three years ago and is in complete remission. She is taking low dose Revlimid maintenance. **Rolf** was diagnosed in December 2013 and took RVD. He is in complete remission and taking 15mg Revlimid with dex. **Gene** had two transplants at Northside eight years ago and is on Revlimid 5 mg. maintenance.

ASH Updates

Dr. Lonial introduced the research team from Winship. Although the researchers haven't met the patients, they appreciate them as they work with the clinical team behind the scenes to advance the research. Dr. Lonial said that there was a lot of information at ASH with over 800 abstracts submitted. Clinical trials on new combinations of drugs were entering Phase II and III. This will bring them closer to approval by the FDA. Dr. Lonial reviewed the steps in the development of new drugs. Step 1 – Identify a Therapeutic Target, which defines the process the drugs will use to attack the cancer. Step 2 – Validate anti-tumor activity in laboratory and animal models, which confirms that the process works as expected. The research uses MM marrow cells to identify the response on samples. Winship has 170 samples and appreciates the contributions of patient to further their research. Step 3 – Clinical Trials: Phase I is for safety and to find the best dose; Phase II is for efficacy to find if the drug is effective against the disease; Phase III compares the new drug with the best available therapy.

The Role of Clinical Trials: Translate basic scientific research into strategies and new drugs to improve patient outcomes; Contributes to progress against cancer; The more people who participate, the faster research questions will be answered; Important for patients and physicians to participate. Dr. Lonial advised patient to not be afraid of clinical trials. The best results are happening in Phase I and patients can gain access to the latest advances from research. Dr. Lonial reviewed MM basics as the disease progresses from **MGUS** to Smoldering (**SMM**) to **Active MM**. Since there are more trials involving high risk SMM patients, the IMWG has re-defined Active MM

to include Free Light Chain (**FLC**) Assays and whole body MRI or PET/CT scans. This will better identify SMM patients who will more likely advance to Active MM and should consider earlier treatment before serious damage occurs. Most clinical trials target relapsed or refractory MM patients (**RRMM**). Dr. Lonial provided definitions: Relapsed myeloma: MM recurred *after* a response to therapy; Refractory myeloma: MM progressing *despite* ongoing therapy. Dr. Lonial defined the terms used for clinical trial results. **ORR** (Overall Response Rate) identifies patients with a response to a treatment that yields a complete response (**CR**) or very good partial response (**VGPR**). This group has no M-protein or the M-protein decreases by 90%; also the percent plasma cells in bone marrow is less than 5% and no new lesions are detected. **PFS** (Progression Free Survival) is the survival time without any increase in the myeloma markers. **OS** (Overall Survival) is survival time, including death from any cause. As research and survival rates have been tracked for a number of decades, the improved ORR from the new drugs is steadily increasing, with **RVD** (Revlimid, Velcade, and Dex) giving a near 100% response. One group of patients with both early and late transplants, including genetic risks, started with RVD and achieved a plateau, where the disease remained at a steady response level for an extended period. The plateau of no disease progression may be considered a "functional" cure controlled by new maintenance protocols. This is to be further defined by new testing and tracking of these patients.

Dr. Lonial then reviewed several clinical trial results presented at ASH. One Italian trial showed significantly higher ORR for VTD (Velcade, Thalidomide, dex) over Velcade, Cytoxin, dex. Another European trial compared the effect of age on outcomes for Rev/dex vs. Melphalan and Prednisone with Thalidomide. The group over age 75 and the group under age 75 each had better results with Rev/dex. A US study with RVD at induction, then Rev maintenance for transplant-ineligible patients, showed a 27% ORR after just four cycles. The conclusion from trials is: IMID + PI (Revlimid (IMID) and Velcade (PI) or their next generations) combination remains the best we have at the outset; 4 drug combinations are coming, with mono-clonal anti-bodies; role and timing of transplant trial continues but current data continue to support the OS benefit for transplant.

Dr. Lonial took questions, the first about MRD testing. He said that about one fourth of patient in complete remission are MRD negative, but there is not enough data to determine the differences and identify who will relapse. IMPACT is the trial for MRD testing and researchers are working to build a database of test results to gain insight. A question about genetics indicators for MM was asked. Dr. Lonial said that BRAF is a mutation common in other cancers, but other cancers have a single driver. MM is more complex. Sequencing MM for new trials is underway. What are maintenance alternatives if Revlimid causes a rash? Velcade is an option given every other week. When oral Velcade (Ixazomib) is approved, that will be a good option.

Dr. Heffner then spoke about monoclonal antibodies. He noted that there are more new drugs. Treatment is getting more complex as doctors are trying to determine which drugs to use and in what sequence. Mono-clonal antibodies may change the course of treatment. Dr. Heffner cited Phase I and II studies of BT062 with Rev/dex, an anti-CD138 antibody. The trials were for RRMM patients, most had previously taken Revlimid and Velcade. There were mild side effects of diarrhea,

fatigue, and nausea. The ORR was 78%, which is good news for these patients who had up to 11 prior therapies, with a median of three regimens for the group of patients. Another Phase I trial with SAR650984 and Rev/dex, an anti-CD38 antibody, included similar RRMM patients. The ORR was 58% with only 4% of patients experiencing disease progression. Dr. Heffner next presented results from a Phase I and II study of Daratumumab with Rev/dex, an anti-CD38 antibody, for RRMM patients showing an ORR of 87%. After four cycles, 60% had VGPR or CR and that increased to 65% after six cycles. Final results of Elotuzumab, Phase I and II, with Rev/dex for RRMM patients was presented with an ORR of 84% and time to first response was one month. Most of the patients (82%) had a transplant and the average time since diagnosis was 4.8 years. In Phase II, the median time to progression was 32 months at the lower dose. These are very encouraging numbers for all the antibodies.

Dr. Nooka presented two abstracts from Phase III PANORAMA 1 study. This study uses Panobinostat with Vel/dex for RRMM patients vs. a placebo with Vel/dex. In part 1 of treatment, patients received Velcade/dex twice a week. In part 2, the Velcade/dex was reduced to once per week. In part 1, the ORR was 61% for Pan/Vel/dex vs. 55% for Vel/dex. Conclusions from this study were that patients on Pan/Vel/dex had better outcomes and side effects were reduced in part 2. Dr. Nooka reviewed clinical trial results from two oral proteasome inhibitors. The first was Oprozomib, which had an ORR of 31% as a single agent. Results are expected to be higher in combinations with other drugs. Side effects included diarrhea, nausea, and vomiting. The other oral proteasome inhibitor is Ixazomib, also known as MLN9708, which has been in Phase I as a single agent and Phase II with Rev/dex and also as continuous maintenance. Major side effects were skin disorders, diarrhea, fatigue, and nausea, but these were much lower when used as maintenance. "RID" is the new combo of Rev/Ixazomib/dex and it shows that 90% of patients achieved PR or better, with CR rate of 22%. Patients stayed on Ixazomib alone for up to 2 years and 48% showed increased response. Rate of CR+nCR increased from 24% after induction to 62%.

Dr. Kaufman talked about combination drugs for relapsed MM. In 2012, a clinical trial with Velcade, Thalidomide, and dex showed that results were superior to Thalidomide and dex alone. Three drug combinations have been more widely used and show improved outcomes. A Phase III trial with Kyprolis and Rev/dex vs. Rev/dex showed an ORR of 87% with KRd vs. 67% with Rd and more patients achieved $\geq$CR (32% vs. 9%). An unprecedented median PFS of 26.3 months was achieved with KRd, nine months more than with Rd. OS at 24 months was 73% with KRd versus 65% with Rd, and it also worked well on high risk patients. A clinical trial with CAR/PAN/dex had ORR of 46% will lead to future combinations with PAN (Panobinostat). A study with Pomalyst/Cytoxin/dex vs. Pom/dex had an ORR for Pom/Cy/dex of 65% vs. 39% for Pom/dex. Another study with Pom/Vel/dex had an ORR of 85% with VGPR or better at 45%. After 8 cycles, Vel and dex were stopped and Pom continued alone. The median duration of response was 14 months. These studies show that three-drug combinations are giving great results and there is more to come!!

Q&A –

Q -Were there any studies on maintenance? **A** – No studies on maintenance at ASH. In the New England Journal, study results show that patients should stay on Rev maintenance as long as tolerated. **Q** – Is the lowest Rev maintenance 5 mg? **A** – Yes. **Q** – Why does MM mutate around drugs? **A** – That is what cancers do to survive. Plasma cells make immune systems for all our lives, so the same happens when cancerous. **Q** – Are heart issues a side effect of Cytoxin? **A** – These treatments are lower dose and lower side effects. Heart problems are rare, but they occur in Kyprolis. One in twenty have serious side effect with heart problems. There is a 2% higher risk in Kyprolis/Rev/dex versus Rev/dex for heart problems. **Q** – Is there a way to work around muscle spasms from Rev? **A** – We do not understand why this problem occurs. Low electrolytes, magnesium, or calcium levels may have an impact. It is important to maintain hydration including Gatorade and tonic water. **Q** – Is alcohol allowed on Rev? **A** - Yes, with moderation! **Q** – Is peripheral neuropathy (PN) permanent? **A** - We hope to get away from PN and most is not permanent. There are not good meds for PN. **Q** – Does drinking alkaline water have an impact? **A** – No. It is very difficult to change the Ph of the body. As far as alternative options, we know that vitamin C and green tea interfere with Velcade. If you don't know what impact something may have on treatment, then don't do it. **Q** – What is the treatment difference for high risk MM patients? **A** - At Emory, 15 – 20% of patients are high risk. Up front treatment is not different. When in remission, treatment needs to be more aggressive for high risk. **Q** – MM is an equal opportunity disease. Is there any difference in treatment or response by gender or ethnicity? **A** – No difference in treatment. Response is about access to medications and FISH. Based on a study of 1000 African Americans, the average age of diagnosis is about ten years younger. Study of this data is continuing to detect differences. **Q** – MM is lower in India. Is that due to turmeric or curry in their diet? **A** – Asian levels of MM are lower in general and Africa is higher. Curry is not easily absorbable. **Q** – Any new answers on genetics or causes? **A** - Doctors understand genetics more to see the difference in patients and identify new mutations. No answers on causes. No good evidence on hereditary link. MGUS in families may be due to shared exposure. **Q** – Is there a cut-off age for clinical trials? **A** – No.

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Southside Meeting Notes, January, 2015

The **February** meeting will feature Kim Nickels, Patient Access, Education and Advocacy Director, The Leukemia & Lymphoma Society (LLS). In **March**, Tammie Rabern from Takeda Oncology will be our guest speaker.

Guest Speakers- Licensed Clinical Social Workers **Alice Mullins** and **Hilary Cohen** are both Hematology Social Workers with the Emory Winship Cancer Institute (ECI) of Emory University. They began by describing the education and credentials of the hematology social worker—they typically have a master's degree in social work (MSW), with special training/credentialing in health

care and are licensed by the state. This training provides the added title of, **licensed medical** or **clinical** social worker. Most Cancer treatment centers have L**M**SW or L**C**SW. Generally, patients are referred to a social worker by the medical team. Usually, Bone Marrow Transplant patients at Emory are scheduled to meet with a Social worker in preparation for the transplant. **Patients can always request to see a Social Worker.**

Some of the information and resources the Social Worker can provide include: (1) **Prescription Assistance programs** --Most pharmaceutical companies have a patient assistant program that will assist patients with medication cost and possibly health insurance reimbursement. (2) **Lodging** –the social worker can help identify lodging for those who live a distance from the hospital where they receive care – this is usually for patients who live 30-40 minutes away. (3) **Transportation**—there are very limited resources for transportation; more resource are available if you are a senior. Still, ask the LMSW -- options change from time to time. (4) The LMSW serves as an **Advocate** for **Medical** and **Community Assistance-**The LMSW provides information about caregiver agencies, community support groups, Legal Aid, Food banks, Utility assistance, etc. Letters for rental agencies and court systems may also be obtained. (5) **Social Workers Conduct Assessments -- risk assessments** to determine a patient's need. They may provide hospice education. Alice and Hilary recommend patients and families have a "working "knowledge of hospice because understanding the concept can help identify when hospice is appropriate. The Social Worker can refer the patient to the Palliative team that will help to take care of pain, and provide other supportive oncology services. Patients should speak with doctor about Palliative care needs. The LMSW will also help assess if referrals to a Psychiatrist or counseling services are needed. (Winship has its own Psychiatric and behavioral Counseling team.). These services are free. You can also be referred to counselors close to where you live.

They provided information regarding **Social Security Disability benefits and MM.** If your symptoms are severe enough, you may qualify for disability benefits, including Social Security Disability Insurance. MM confirmed by appropriate serum or urine protein electrophoresis and bone marrow findings will determine eligibility for Social Security Disability. You will qualify for disability if you have multiple myeloma that doesn't respond to treatment or continues to progress after a full course of initial treatment or if you have had a stem cell or bone marrow transplant within the past 12 months. Thereafter, they will evaluate any residual impairment(s) under the criteria for the affected body system. **Social Security will look** at the combination of all of your symptoms, test results, and impairments and how they affect your ability to work. They will also consider your age, education level, and work experience to determine if you should be deemed unable to work. For more information, call **1-800-772-1213 or apply on line ssa.gov.**

Finally, Alice and Hilary encouraged us to down load the **Georgia Advanced Directive for Health Care.** This instrument will communicate your intentions regarding how your health care should be handled. In addition to providing the completed form to your doctor and/or health care agency, we should discuss details with family.

The Emory Winship Social Workers host an **Oncology Hematology Support Group** that meets on the second Tuesday of each month from 1 pm to 2:30 on the first floor of Building C, at Winship– they provide a voucher for parking. **Peer Partners** is a program offered at Winship that matches patients with survivors to make telephone communication. **Peer Partners** is looking for volunteers. They can be reached: Alice- 404-778-5559 and Hilary-404-778-5535.

Some **often requested resources** for medical assistance include: Prescription assistance programs www.needymeds.org and www.goodrx.com. The Cancer and Career (www.Cancerandcareers.com) website empowers and educates people with cancer to thrive in their workplace by providing expert advice, interactive tools and educational events. Cancer and Careers strives to eliminate fear and uncertainty for working people with cancer.

In Case of Emergency (ICE): Debra VA Oncology Nurse and consultant to our support group, encouraged us to add our emergency contact person(s) in our cell phone. She shared that a friend who lived alone, passed away. Several days passed before anyone was aware. She sad if you live alone you should have a communication system that includes talking with someone each day—a buddy system. She also had each of us to update our cell phones with an **In Case of Emergency (ICE)** contact. She suggested that we keep the cell phone with us even in the house in case of a fall, etc.

MM Month plans. Alma reported that since Greenbriar Mall will host a health fair on **March 28th** our - myeloma awareness campaign will become part of that effort. In addition, we will submit articles from IMF to local newspapers for printing and distribution. We will also contact municipalities that have not yet provided proclamations for Myeloma Awareness. **Alma** is looking for radio contacts to expand MM awareness. Also, add to your calendar the annual Health Fair Sponsored by Delta Sigma Theta, Inc. will be held on **April 25th at** Greenbriar. We will need volunteers to man tables for both health fairs.