Northside Meeting Notes - January 2014

Northside meeting was held at Winship Cancer Institute

Winship ASH Review – January 4, 2014

Charise Gleason reviewed the journey of new treatments through clinical trials to approval. Pre-clinical research (before human trials) takes an average of four years. Phase I takes two years, Phase II two years, and Phase III is three to four years. New Drug Application (NDA) until FDA approval is about a year. **Phase I** is "Bench to Bedside" when new drugs are tested for a safe dosage and how it is administered. This includes 15 to 30 patients and side effects are closely monitored and effects graded watching for Dose Limiting Toxicity (DLT). **Phase II** involves up to 100 patients and uses the dosage from Phase I to evaluate for effectiveness. The endpoint is response to the treatment resulting in **sCR** (stringent complete remission), **CR** (complete remission), **VGPR** (very good partial response), **PR** (partial response), or **SD** (stable disease). Watch for these terms later in this document. **Phase III** may recruit 100 to 1000's of patients to evaluate the new treatment compared to the standard of care. These studies usually randomize patients at multiple locations. Eligibility criteria are less stringent than prior phases. The good news is that treatment options have greatly increased in last 12 years as a result of new drugs in clinical trials.

Cathy Sharp talked further about clinical trials bringing new drugs and new combinations of drugs to increase effectiveness against MM. Winship currently has available 33 studies with patients, 15 of which are open and actively recruiting, including some with MGUS patients. Four studies involve tissue samples and ten studies are in the pipeline to be open in 3 – 6 months. How can a patient participate in a clinical trial? Talk to your doctor to get a referral to Winship for evaluation. If selected, carefully review the consent form and ask questions about the protocol and procedures. Patients should still see their oncologist and primary care doctors, because the investigators are collecting information only about the study. The MM team meets every week to discuss all patients in the studies and their side effects. Side effects are closely monitored and measured. Important facts about Clinical Trials: participation is voluntary; no one will receive a placebo since the new drug is compared to the accepted standard of care; patient health and safety is a priority; the patient may discontinue in the study at any time. Benefits of Clinical Trials: access to the newest treatment; you have an active role in your healthcare; you receive regular and careful monitoring; and you will be helping others gain access to new treatments.

At ASH, Emory received the MMRF Accelerator Award and they opened the first trial site for Daratumumab (monoclonal anti-body) and had nine patients on the new treatment before other sites opened. Dr. Lonial also participates on the International Myeloma Working Group (IMWG) that sets the standard of care worldwide.

Dr. Anand Jillela is new to Winship, coming from the Medical College of Georgia, and is studying the early stages of MM – **MGUS** and Smoldering MM (**SMM**). MGUS is defined as protein levels less than 3 grams and plasma cells in the bone marrow less than 10%. SMM is identified when protein levels are greater than 3 grams and plasma cells more than 10%, yet there is no bone or organ damage. Progression to MM usually occurs within five years. Previously, care for SMM was to monitor regularly. There is now a Spanish study comparing treatment to observation. After three years, the treated patients took longer to progress, but it may be several more years before final results are available. Emory has a study treating SMM patient with high risk factors and it shows benefits in 37 out of 44 patients. The study is moving to the next phase. For low risk SMM patients, observation may be a reasonable approach.

Dr. Ajay Nooka has been involved in the clinical trials at Emory for a couple of years and reported on a study with continuous Revlimid and low dose Dex for newly diagnosed patients ineligible for transplant. This study has 1623 patients at 246 centers in 18 countries. This study has three arms for comparison: Arm A is Rev/dex until the disease progresses; Arm B is Rev/dex for 18 months; Arm C is Mel/Pred/Thal for 72 weeks. After 37 months, 50% are still on the trial. Important information from this study is about secondary primary malignancies (**SPM**) which is secondary cancers suspected to be caused by treatment. In this trial, SPM rate was very low in Arm A and B, which are the ones without Melphalan and Prednisone. Since the patients did not have a transplant, they were not exposed to high doses of Melphalan. After 3 years, the progression-free survival (**PFS**) was 42% for Arm A vs. 23% for the other two. Four year overall survival (**OS**) was 60% for Arm A vs. 55% for Arm B and 50% in Arm C. Dr. Nooka mentioned several other studies that are underway at Emory.

Dr. Tom Heffner has a long tenure at Emory and has seen many of our group's members. He talked about an "all oral" trial with MLN9708 (oral Velcade, aka Ixazomib) with Revlimid and dex in newly diagnosed patients. The final data from Phase I and II has been made available. Phase I had 64 patients and there were no DLT at either of the trial dose amounts. Phase II used MLN9708 at the lower dose of 3 mg, since the higher dose caused a rash in most patients. The overall response rate (**ORR**) was 94% with 76% gaining CR or VGPR. Data showed deepening response over the course of treatment. The same results were achieved when the dose was reduced from twice per week to once per week. The adverse events (**AE**) at grade 3 were rash at 16% and neuropathy at 5%. There were no AE's at grade 4.

Dr. Heffner also talked about a trial BT062 for relapsed and refractory myeloma (**RRMM**) patients using Indatuximab (monoclonal anti-body) with Rev/dex. Grade 3 or higher adverse events were very low and it showed a 75% ORR for RR patients. Results of stable disease (disease did not progress) or better was 100% and the treatment was well tolerated for up to one year. The MM community is excited about the anti-bodies, which is a new type of drug compared to those currently available, and FDA approval on one of the versions may occur in 2014.

Dr. Jonathan Kaufman spoke about studies for relapsed and refractory MM patients. The first study discussed used Carfilzomib (Kyprolis) with Pomalidomide (Pomalyst) and low dose dex. There were 79 patients involved, with an average of 5 years since diagnosis and an average of 5 prior therapies and 90% refractory to Revlimid. The ORR was 70% for all risk levels with 25% VGPR or better, independent of risk factors. Response rate for Car alone is 25% and Pom alone is 33%, so this demonstrates what the researchers have known about combining drugs, is that 1 + 1 = 4!! Another study that Dr. Kaufman reported on is the ARRY520 in RRMM patients. This is another new type of drug that inhibits the KSP protein. It had ORR of 33% as a single agent and is expected to do much better in combinations.

Dr. Kaufman talked about the Daratumumab study with Rev/dex in Phase I and II. It was well tolerated and 8 of the 11 patients have responded. SAR650984 is another anti-body in Phase I trial as a single agent. The first results show ORR at 30 – 40%. There were infusion reactions that subsided after the first cycle.

Dr. Sagar Lonial talked about the role of transplant in MM treatment. The current standard is a three-drug induction then transplant. Maintenance therapy extends the duration of first response. Trials are now starting to measure Minimum Residual Disease (**MRD**). This is a new level of testing to find MM cells that may not have been previously detected when a patient is in remission.

There is a trial at Emory with newly diagnosed patients getting the same induction therapy then the group is divided into early transplant vs. delayed transplant when the disease relapses. There is a study in Italy comparing transplant vs. no transplant then maintenance vs. no maintenance. The

conclusion is that transplant is still a vital component of MM therapy and critical for lower levels of MRD.
Panobinostat is a HDAC inhibitor, another new type of therapy, in Phase I and II trials with Vel/dex under the name Panorama. Previously, trials were done with Vorinostat, an earlier version, but it was determined to be too toxic. Panobinostat is not showing the same toxicity. ACY-1215, a new HDAC inhibitor, took only 2.5 years to get to clinical trials. This was due to collaboration between research centers and involvement of LLS. This is showing an ORR of 69%.
Conclusion from Dr. Lonial: the role of transplant is still valuable to achieve MRD negative; continuous therapy, when tolerated, is recommended for better outcomes; new targets and drugs are on the way to personalize MM therapy; genome sequencing on MM patients will show targets for new drugs. More selective 2nd/3rd generation drugs with better toxicity profiles were presented at ASH. We are now in a rapid learning phase.

Q&A:
Can the genetics of MM in a patient change over time? Yes, especially after transplant and extended treatment.
How is peripheral neuropathy measured? Common Terminology Criteria for Adverse Events (CTCAE) version 4, as set by the National Cancer Institute. This provides a standard for measuring conditions and symptoms then grade them 1 – 5.
What is the determination about the role of maintenance? US and Europe disagree on the length of maintenance. Europe provides Revlimid maintenance (10 – 15 mg) for only two years and in the US it is given until the disease progresses. In Europe, it is given continuously, while in the US the dose is 21 days on and 7 days off.
What is the status of MRD testing? Dr. Lonial will be working this year with IMWG to set the standard of testing for MRD. It is available now at Emory, but the patient must request an additional sample be taken for Dr. Lonial.
Please comment on gene therapy. Dr. Lonial answered in reference to CARS antibodies: the data is still early for MM, but appears more promising in lymphomas.
What will change in Winship treatment as a result of the information from ASH 2013? Dr. Lonial said that the information at ASH demonstrates that the care at Winship is at the leading edge and will be discussed at ASH next year. Dr. Kaufman said that Winship practice of using Rev for maintenance was confirmed for longer PFS. Also, if a transplant is tolerable, it should be included in the treatment plans. Winship is excited to be involved with the new drugs that are showing great results, especially for relapsed MM patients. It is great for patients to have more options.
What are guidelines for a second transplant? If the duration of remission after transplant is less than two years, then a second transplant would not provide benefit. Maintenance is key to PFS. However, if blood counts are very low and not recovering, a second transplant may be considered to reset the marrow.
Was there any news about Complementary Treatments? Charise said that there was not a lot at ASH.
Does age play a role in maintenance therapy? Only thing is younger patients can better tolerate it.
Does cytogenetics (FISH) play a role in maintenance? One of the differences is that Winship has implemented a quicker staging after transplant, at day 60 for high risk patients instead of day 100.
If a patient is not treated regularly at Winship, how is that patient able to participate in clinical trials? Work with your oncologist and if MM numbers increase, then ask for a referral to

Winship before beginning maintenance or new therapies, in order to be considered for a clinical trial.

Is there benefit to screen for secondary cancers? Screening for common cancers thru routine health maintenance makes sense. But the incidence of secondary cancers from MM treatment is such a rare event that it doesn't make sense to specifically screen for those.

Respectfully submitted by Nancy

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Southside Multiple Myeloma Support Group Meeting -- January 25, 2014

Gail called meeting order. There were (about) 17 people present (some latecomers did not sign in). We welcomed **William** back to the group he was living in Chicago for several years and recently moved his work back to Atlanta.

The group brainstormed on the 2014 calendar and identified a list of topics and speakers to present during Support Group Meetings. Some topics of interest included: March – Understanding Lab Values (everyone should bring detailed lab results from several visits and know other information about their MM -- IgG, IgA, IgD, IgE, paraprotein/Bence-Jones protein, free light chain levels, etc.); Immunologist - Speak on what patients can do to strengthen our immune system; Adverse side effects from drugs -- Revlimid and other Chemo drugs side effects; field trip to the new Cancer Centers of America site in Newnan; archived webinars from IMF and LLS (after we get projector); Complementary and Alternative Medicine (CAM) – role of nutrition, vitamin supplements, herbs in control of MM; more on Clinical Trials; Patient/Doctor Communication; increasing our membership; Personalized medicine/genomics. We will try to get **Vermell** to speak about Lab Values in March. **Alma** will try to get Celia for February or April meeting.

Doris, Vermell, and Gail attended the session at Emory on the Best of ASH 2013 (American Society for Hematology). There was lots of information on results from studies on maintenance therapy (Lonial and others report the survival rate for those on Revlimid maintenance is better than those not on maintenance); emphasis in research is on getting to minimal residual disease (MRD) – there are new definitions for Complete Remission (CR); new drugs are on the way to personalize myeloma therapy – with studies in gene sequencing; personalizing gene therapy includes "P53 deletion and 4:14 translocation" – the COMMpass study is a 10-year multicenter trial recruiting newly diagnosed myeloma patients seeking to conduct genetic analysis for more effective treatment; fast moving drug approvals. There was not much on complementary medicine at ASH. There was nothing new to report on the study with African Americans to help determine why MM is more prevalent in blacks. Find more details in the January 2014 newsletter.

New Member: Elizabeth was diagnosed in 2007 at Atlanta Cancer Care Towers. She has only one kidney – kidney removed because it was cancerous. That is when the myeloma was discovered and received care at MD Anderson in TX. She was on Velcade (resulting in neuropathy) and ended up at St. Joseph's hospital for 10 days. In 2010, she was in bed for most of the year. She had blood work in Stockbridge and was seen by Dr. Sedu. He stopped the Velcade, prescribed physical therapy. She is now on 15 mg Revlimid. She was referred to Dr. Lonial at Emory, but is concerned that she never sees Dr. Lonial – "only" a nurse or someone else. **Alma** noted that she had been referred to Dr. Lonial from a general oncologist. She saw Dr. Lonial for the first 2 years, but now sees nurse practitioners and watches her numbers (free light levels). If there is a change in her care, she always

can see Dr. Lonial. Elizabeth said she was paying hundreds of dollars per month for medications that she could not afford. **Alma** offered to assist her in obtaining assistance from the drug companies and other sources.

Gail, Pat, and others offered that there is a "myeloma team" consisting of doctors, physician assistants, nurse practitioners, researchers, clinicians, and social workers, all are well qualified professionals. They jointly review all patients' cases. If your myeloma is stable, the doctor might be needed to spend time with others. Anytime you want to see a doctor, call and schedule the time with him/her in advance. The reality is that some patients/doctors personalities do not gel…same with co-workers, or even family members. The most important question is -- do they spend their considerable talents to give you the best possible care? The doctor is only as good as their ability to communicate with the patient (not considering "House"). Discuss concerns with doctor – and change if needed. There is too much stress in living with cancer, not to have full confidence in your doctors. **Update on Carl:** Carl is no longer on medication and continues to do well. Carl began drinking tea made from the Cerassee plant root and found that his M-protein levels went from .29 to 0. He takes 1 once of the Cerassee plant and boils in 1 quart of water. He steeps tea for 30 minutes and strains. The cooled tea is stored in a glass bottle and he drinks 6 ounces once or twice per week. **Cerassee can be toxic to liver and has not been proven to cure myeloma.**

Other discussion

Janet was diagnosed with MM in 2012. She was being treated at Atlanta Cancer Care/Lawrenceville. She stopped maintenance of 10mg Rev after developing rashes & lumps. This was eventually identified as (cutaneous) mycosis fungoid the most common type of T-cell lymphoma/non-Hodgkin lymphoma (this affects the skin, but might progress internally over time). Symptoms include rash, tumors, skin lesions, and itchy skin (Source: NCI, NIH). **William** also had rashes that he thought were related to acyclovir. He is now on no medications. **Janet** shared there is an article on Survivorship in Cure Magazine -winter quarter, "Why do Drugs Stop Working." The magazine is free and available online http://www.curetoday.com/index.cfm/fuseaction/magazine.show/id/15. There is another article of interest on the importance of patients setting goals during treatment with providers to determine the finish line. Still another article of interest is in the Journal of Oncology - 2014 "Should I Fire my Oncologist?" It is important not to "suffer in silence" during treatment. You should develop a trusting relationship with your health providers. We should invite health care worker to speak on Patients' Rights. Many patients can get their medical records online/electronically, and communicate via email with doctors. Find out if this service is offered by your providers, and consider using it for your benefit.

Myeloma Awareness Month

Alma is spearheading the South Side Myeloma awareness month campaign. She needs help identifying and locating mayors in various municipalities on the Southside of Atlanta. She is planning to have Proclamations made from each municipality. So far she has identified 9 mayors: Union City, Fairburn, East Point, College Park, Fayetteville, Hapeville, and Riverdale, Morrow, and Jonesboro. **William** and **Doris** volunteered to participate on this project with Alma R. leadership. **Pat** suggested a walk or some sort of physical activity for Myeloma Awareness Month that will engage the community. There was discussion that the group could organize a Tai Chi gathering to be convened in the Greenbriar Parking Lot. **Gail** suggested placing an article in the What's Going on section of the AJC, the Cascade Patch and the Atlanta Daily World. She also suggested this is another opportunity for folks to write up their myeloma journeys – diagnosis, survivorship, etc.

Advocacy

Georgia, South Carolina, & North Carolina will introduce legislation this session to support HB 1801- (Oral Parity) and HB 460 (Specialty Tiers). Rep. Lee Hawkins from Gainesville, District 27, will sponsor the Georgia legislation. Call and Email your representatives TODAY! It's easy to take the call – takes about 2 minutes. They usually do not ask you lots of questions. Example – Gail called the Georgia Insurance Commissioner –about the Cancer Fair Treatment Act -- told the woman who answered..."I am a cancer patient..." she interrupted and said, "I will put your name on the list -- we have gotten TONS of calls. You all are doing a fabulous job! Keep up the good work." That was it... We will be sharing your postcards with Georgia Assembly members this session. THANK YOU!; The Planning Actively for Cancer Treatment (PACT) Act of 2013, introduced in the House, will provide Medicare beneficiaries a new service by incentivizing physicians to create a written care plan and to discuss and alter the plan based on shared decisions - Ask your legislator to support PACT as well. To find your federal and state elected officials by zip code**, go to: http://www.commoncause.org/siteapps/advocacy/search.aspx?c=dkLNK1MQIwG&b=4860375**

Announcements/Upcoming Education Opportunities:

- **Chemo Brain – Free teleconference** to Kick of Myeloma Awareness Month!! International Myeloma Foundation presents as part of the Living Well with Myeloma Teleconference Series: **Chemo Brain-Is It Real - Thursday March 13, 2014 7:00 pm Eastern Standard Time - 60 minutes long** Featuring**: Pamela Joyce Shapiro, PhD - Assistant Professor, Depart of Psychology, Temple University** **Pre-Register at: www.Chemobrain.myeloma.org**
- Leukemia and Lymphoma Society - submit forms for financial support. Kim Nickels - new Patient Access, Education, and Advocacy
- IMF - archived from January 16 webinar - Best of ASH 2013 - What Patients Need to Know
- IMF - Veteran's Against Myeloma website - veterans.myeloma.org provides links to relevant Veterans Administration information, such as state veterans assistance offices and national veterans service organizations.
- Affordable Care Act and you - http://cqrcengage.com/myeloma/app/register?1&m=10399 - What myeloma patients should know about insurance options-healthcare.gov
- IMF Patient & Family Seminar will be held at the Marriott Hotel in Buckhead near Lenox on May 16th & 17th 2014. Registration to attend the seminar is available via the IMF hotline 800.452.CURE (2873); or online. Costs before April 15 are available for one day $30 or both days $60. After April 15 are $50 –Friday only, and $85 (for both days). http://myeloma.org/EventPage.action?tabId=7&queryPageId=4&eventCategoryId=1&eventId=687

  The group decided in the future, we should routinely open the meeting with a moment of silent meditation and/or breathing exercise; then closes the meeting with words of inspiration.

  Respectfully submitted by Gail and Paulette