December 2016

**Northside Multiple Myeloma Support Group Meeting**
**December 3, 2016**

## Business

December meeting was our traditional Holiday Party with tasty dishes from our members and lots of time to visit with each other. We also collected toys for Children's Healthcare of Atlanta to give to the kids in the hospital during the holidays. We collected 64 toys!!

**The AAMMSG Board of Directors** met before the general meeting and worked on the programs for 2017. There will be a survey going out to the members in January asking about programs and how the group can meet your needs. One of the announcements from the Board is that Joe Brown has stepped down as co-leader of the group. Jim Mahoney has agreed to take his place in assisting in the leadership going forward. Thanks to Joe for ten years of service! We have several committees that help keep this group running smoothly and a couple of them are in need of assistance. The Outreach committee needs two more people to do occasional phone calls to patients who are unable to attend meetings. The Refreshment committee needs someone to help with scheduling and reminders. These requests involve minimal effort, but make a big difference for the members of the group. Please consider helping and connecting with other members. Reach out to Nancy or Sandy if you can help.

## ASH Review at Emory – Dec. 10, 2016

There were over 60 people gathered in the conference room at Winship to hear the latest from the ASH meeting in San Diego. The meeting started with Charise Gleason giving an overview of clinical trials and some of the abbreviations. She reviewed the timeline of clinical trials. The pre-clinical testing, after a new drug is identified, can take four years before an Investigation New Drug Application can be made to the FDA. Then Phase I and Phase II trials take about two years each and Phase III trials take 3-4 years before a New Drug Application to the FDA. Approval of the drug can take up to a year, so this is eight years minimum for a drug to get approved. There are rigorous and expensive rules and controls each step of the way. Some drugs don't make it through the clinical trials if they don't show significant improvement in outcomes. Phase I of clinical trials is to determine the appropriate dose for further evaluations. Phase II is to determine if the agent has activity against a specific cancer type. Phase III will determine if a treatment is effective. Phase IV is after FDA approval and has various goals. Some of the terms used in clinical trials are:

- Stable Disease (SD)
- Minimal Response (MR)
- Partial Response (PR)
- Very Good Partial Response (VGPR)
- Near Complete Response (nCR)
- Complete Response (CR)
- Stringent Complete Response (sCR)
- Progressive Disease (PD)
- Overall Response Rate (ORR)
- Progression Free Survival (PFS)
- Minimal Residual Disease (MRD)

For just Multiple Myeloma, Emory has 37 studies with active patients, 17 studies open and actively recruiting, 115 patients currently enrolled on studies, 4 Tissue bank studies, and 25 studies in pipeline. This is amazing and we realize that we are so fortunate to have such a center of excellence for Multiple Myeloma here in Atlanta. Charise wants the group to know important information about clinical trials:

- gives access to new therapies; participation is voluntary;
- you will not receive a placebo;
- your health and safety will always be a priority;
- you may discontinue at any time.

When you are on a clinical trial, you are closely monitored and all side effects are recorded and graded. This is important information for the clinicians and future patients.

**Q:** What is the meaning of "off-label"? **A:** The FDA approves drugs at certain dosage levels and may specify them in combination with another drug. If you start out with that program but have reactions, the dosage or combination may be adjusted to "off-label" amounts, schedule, or combination. Another example is Nivolumab and Pembrolizumab are lung cancer drugs that are being tested in Myeloma.

Dr. Lonial presented results from some clinical trials that he thought would be important for the group. He used the analogy of an iceberg where the tip of the iceberg is the initial diagnosis. The bulk of the iceberg is below the surface as the bulk of treatment continues toward remission and possible cure. The hot topics are MRD (Minimal Residual Disease) and immune therapy. MRD is the new testing to find MM cells when the patient is in remission and determine what treatment will further reduce the disease. We all know that the disease can relapse, so the goal is to stretch out the first response as long as possible. This is when the disease is most receptive to treatment. The goal now is to achieve MRD-negative, where no MM is detectable. Patients may still relapse, but the remission is longer and some studies are showing longer OS (overall survival). There are two versions of MRD testing. One is NGF (Next Generation Flow) which is a new flow test done on the bone marrow to find one MM cell in one million (or more) marrow cells. The other is NGS (Next Generation Sequencing) which does the genetic sequencing of the MM cells to find abnormal patterns. Both of these processes hope to define identifiers for treatments guidelines, remission levels, and eventually measure a cure where treatment can be discontinued.

One clinical trial of interest was comparing VRd (Velcade, Revlimid, low dose dex) with Rd in newly diagnosed patients. After eight cycles, patients went on Rd maintenance until relapse or toxicity caused withdrawal. The three drug group showed a higher OS with a median of 75 months vs. 64 months. Another trial used KRd (Kyprolis, Velcade, dex) at initial treatment then compared the difference for the groups that had a transplant with those who did not have a transplant. The PFS was better in the transplant group: 86% vs. 72% after 50 months, but the OS was not significantly different. With KRd and transplant, there was a very high ORR and MRD-negative rates, but the toxicity rate was higher with blood clots and heart failure. Dr. Lonial said that there are concerns with moving this study forward in a larger scale. Another conclusion from studies is that improving induction (initial treatment) can improve the outcomes from transplant. It can improve outcomes for high risk MM and may lead to higher cure rate among standard risk patients. Dr. Lonial cautioned about presuming all CRs are the same. The goal now is to achieve MRD-negative.

An important trial is using RVd induction, harvesting stem cells, and one group going to transplant while the second group gets transplant on first relapse. The results show longer remissions if the patient achieved MRD-negative in either group, regardless of transplant timing. More remissions were achieved in the transplant group. Patients with negative sequencing did better than patients with negative flow. For now, we can't predict who will get to MRD-negative, so transplant is recommended for all those who are eligible. Dr. Lonial defined the difference between consolidation and maintenance. Consolidation is more intense treatment for a shorter duration and maintenance is less intense for a longer duration.

**Q:** Should a patient be on consolidation or maintenance after transplant**? - A:** Yes, everyone should be on maintenance.
**Q:** How long is the standard for maintenance? - **A:** Since the data shows better outcomes, everyone should be on maintenance for ??. If you are high risk, then should definitely be on aggressive maintenance for three years.
**Q:** Can a patient change to high risk? - **A:** Yes, risk identifiers can change in the MM clones.

Another trial showed no benefit for tandem transplants vs. single transplant after VRd induction. In Europe, tandem transplant showed better results, but their induction was VCd (with Cytoxin instead of Revlimid). This shows that using the newer drugs at induction makes a difference. Another study showed that replacing Velcade with Ninlaro lowers risk with great results and the French think that Ninlaro should be taken twice a week, but more data is needed on both these concepts. At this time, VRd is still the standard for induction.

There is a lot of news on immune therapy and research is progressing to be more targeted. A new class of immune therapy is ADC – anti-body drug conjugate, where the anti-body is delivered in combination with chemo to improve activity. This showed a 66% response rate in patients resistant to five lines of therapy! CAR-T cell receptors are being modified to recognize the cancer cells and reduce impact on the overall immune system. It is very difficult to engineer and grow T Cells, so there is so much more research needed. Approved immune therapy (Daratumumab and Elotuzumab) are being combined with RVd for induction in new trials. This would move to a four drug combo for initial treatment to get the best response for a longer first remission, as discussed earlier. Watch for news about this in June from the ASCO (American Society of Clinical Oncologists) conference. Another immune therapy is BiTE – *Bispecific T Cell Engager*. This treatment could improve the targeting of the T Cell attack on the tumor without the difficult extraction and engineering process.

**Q:** When will BiTE be available at Emory? - **A:** Some time in February.
**Q:** Will other site have BiTE? -**A:** There are six pharma's involved in this research and they choose the sites.

**Q:** Is Myeloma research and results discussed with other hospitals? - **A:** Emory sets guidelines for treatment and will work with Northside and Piedmont to teach them the therapy options and results, if they ask! Emory is exceeding the national results in PFS and OS, which shows that it is important to get to a center of excellence.
**Q:** Will BiTE be better than engineered CAR T Cell therapy? - **A:** There is not enough data on BiTE, even though it is more practical. Stay tuned for clinical trial results.
**Q:** What defines a relapse? - **A:** An increase of M-spike of 50%, with a minimum of .5.
**Q:** When would a patient evolve to high risk? - **A:** New mutations may appear at relapse. Chromosomes may evolve or lose p53 or 17p after therapy and relapse. The longer a patient is treated and relapses, with 8-9 lines of therapy, then they are considered high risk.
Summary of new directions: IMID/PI induction is standard. Which IMID and PI partner is optimal is not clear. Transplant continues to have an important role in the quest to achieve MRD negativity. Maintenance is not a one size fits all. Four drug induction is on the way (ASCO and ASH 2017). Immune based treatments are here and getting better.
Dr. Nooka talked more clinical trials that were of interest. One was Selinexor in heavily pretreated (5-6 lines of therapy) MM patients, the STORM study. This showed a 27% ORR in these patients, although many dropped out of the trial due to side effects, including low blood counts and anemia. Another drug, Ventoclax, showed a response rate of 40% in high risk MM patients with t(11;14), but only a ORR of 6% in standard risk patients. This was a phase I trial for relapsed MM patients with several previous lines of therapy. A study with Pembrolizumab, Pomalidomide, and dex had a 60% response rate in patients with 2-5 prior lines of therapy. The median duration of response (DOR) was 16.3 months. A study with Daratumumab, Velcade and dex (Dara/Vel/dex) compared to Velcade and dex showed an ORR of 83% compared to 63% on Velcade/dex. Greater than VGPR was 59% compared to 20%, which indicated a deeper response by adding Dara to Vel/dex. Twelve month PFS was 61% vs. 27% with Vel/dex. With only one prior line of therapy, the twelve month PFS rate was 77%. This shows significant improvement by adding Dara to Vel/dex. Another study of Dara with Rev/dex vs Rev/dex in patients with 1-3 prior lines of therapy showed an 18 month PFS of 77% compared to 50% on Rev/dex. The final study presented was with Dara/Pom/dex (Daratumumab, Pomalidomide, dex) for patients who were new to Dara or Pom (Group 1), refractory to Dara or Pom (Group 2), and patients who were refractory to both Dara and Pom. During the study, 46% of patients required a dose reduction of Pom and 22% reduced dex dosage. The ORR in group 1 was 89%, Group 2 was 41%, and group 3 was 33%. These studies show good results by adding Dara to a variety of treatments.
**Q:** Is Dara and Pom used at other centers? - **A:** Dara is newly approved, but Emory has a lot of experience with it. Also, there are more patients at Emory for this clinical trial. Pom is an immune-modulator which enhances Dara's immune therapy. This combination was logical to see if these will enhance each other and work when one has failed.
**Q:** What is the status of the "Blood Biopsy"? - **A:** Blood is less sensitive than marrow. Blood tests are better in solid tumors. Hematology needs bone marrow for a complete assessment. The Blood Biopsy is a "work in progress".
**Q:** How do you work with other doctors outside of Emory? - **A:** Emory will provide a consultation and a treatment plan to be executed by your local doctor.
**Q:** Is there an information network to connect to other doctors for helping patients and providing opinion? - **A:** Hospitals are very competitive and as hospitals are buying up doctor's practices, they would rather send patients out of state than to Emory. Emory wants to see patients and provide a plan that can be treated elsewhere, but the patient must drive the consultation.
**Q:** How do patients get on the newer drugs like Selinexor or Ventoclax? - **A:** If you can get them now only on clinical trials since they are not approved. If you are not eligible for a clinical trial, you can be evaluated to receive them for "compassionate usage".
**Q:** Are monoclonal antibodies for relapse only? - **A:** Trials for newly diagnosed patients have just started. They were approved by the FDA for relapsed patients to have more options. Newly diagnosed patients have an excellent option with Rev/Vel/dex.
**Q:** If a drug is already approved for another cancer, does that mean it can get approve for MM faster? - **A:** That does help, but it is still a long road to approval.
**Q:** What is the maximum number or pre-treatments to be on a clinical trial? I have had MM for 17 years with no remission. - **A:** Some trials have limits or define which class of drug has relapsed, but others have more options. With 25 trials in the pipeline at Emory, it may be worth it to get a consult and explore options. Dr. Lonial mentioned that he is looking for patients in first relapse for some trials.
**Q:** Is Rev maintenance counted as a line of therapy? - **A:** Initial treatment and maintenance equals one line of therapy.

Respectfully submitted by Nancy B.

**Southside Multiple Myeloma Support Group Meeting**
**Saturday, December 24, 2016**

**Meeting Notes**

There was no meeting for the Southside this month.

Please Note: Meeting notes are anecdotal only and not intended to replace advice from your doctor. Feel free to review the discussion topics with your healthcare team.