

August 2015 Northside Meeting Notes

Our guest was Dr. Donald Harvey, a registered pharmacist and Director of Phase I clinical trials at Winship. His personal interest is how an individual handles drugs based on gender, race, age, and other factors.

The new drugs are big news since twenty years ago there was only melphalan or VAD. Now, initial treatment can be three, four, or even five drugs together. The combinations have no more side effects than single agents and are providing deeper responses to avoid drug resistance. Also new are the antibodies that target the way a MM cell grows. Daratumumab showed promising results. Elotuzumab has been submitted for FDA approval. Ixazomib has also been submitted for FDA approval. It is not quite oral Velcade and side effects are more rash and less neuropathy. This is an exciting time with lots of new drugs and new combinations.

Q – Kyprolis is given with Rev and Dex. Why the combination? What if someone reacts to Rev? Can they take Kyprolis alone?

A – Combination of three is better than Rev/Dex, but more side effects. Your doctors will watch the MM response and monitor the side effects. Sometimes, you may need to move to the next generation of the drug to reduce effects. The next generation of Revlimid is Pomalyst, which works differently, and may have reduced side effects.

Q – Prior to transplant, I had RVD with no problems. Now, after transplant, even 5 mg of Rev gives me a reaction. What has changed with the transplant?

A – All side effects are regulated by your immune system. The system learns things, good and bad, with more exposure to the drugs. The more the MM reacts to the drugs, the more the immune system reacts.

Q – So, should I expect the reaction to get worse?

A – Some times when a drug is reintroduced after a period of time, there may be a different reaction. Work with your doctor to change to a lower dose and monitor.

Q – I started on Dara (Daratumumab) a year and a half ago and doing well. The first dose caused a severe reaction, but then things settled down. What was happening in my immune system?

A – Just like Rituxan in CLL, Dara in MM targets CD-38 in the MM cells. When you started Dara, the MM was measurable and active, which indicates a lot of CD-38. When the Dara attacks the CD-38 and the cells die, the dead cells are flowing through your system and causing a reaction. The drug works quickly and creates lots of dead cells, which is a good thing. After the first dose, the volume decreases and there is less reaction.

Q – If someone reacts to a drug, will they have less reaction to the next generation of that drug?

A – We are seeing next generations of drug in many drug classes delivering more effective treatment with less severe side effects. We went from Thalidomide to Revlimid to Pomalyst for the IMiDs. Then, we went from Velcade to Kyprolis for Proteasome Inhibitors (PI), which reduced nerve damage.

The world of drug development goes in two directions, control or cure. For example, Statins are used to reduce high cholesterol, a chronic disease. The real research is to reduce heart attacks and strokes by controlling the cholesterol. In MM, the para-protein causes bone and kidney damage. If you take a drug every day, the protein goes down along with the risk of damage. Same as for high cholesterol as a chronic disease, the goal is to manage the disease. If you take the drug away, the disease is still there and will come back. In MM, the system adapts and the disease becomes resistant to the drugs. Now the approach is to use more drugs up front to dramatically reduce the disease then manage it better to keep the disease down. Like with HIV, patients live normal lives on drugs to control the disease and the researchers are working on drugs to eliminate resistance. Then the research will go for the cure in the long term. Maintenance or Cure? We have to walk before we run, so we have maintenance while we research for the cure.

Q – How does the immune system see cancer?

A – When cells acquire mutations and become cancerous, they can put on a cloak that prevents them from being detected and destroyed. The new drugs remove that cloak so the T-cells can attack it. If the system overshoots the target, the liver and gut will have side effects, but at the same time the cancer is targeted. There are new ways to treat cancers with the immune system that means a cure so that the body can monitor the abnormal cells. Elo (Elotuzumab) works with other drugs and turns on the Natural Killer cells to fight better against the MM.

Q – Are mono-clonal anti-bodies, like Elo, only for certain patients?

A – A good drug will work for all patients. Personalized medicine is a good idea, but a better drug treats all patients without specific or expensive testing. Targeted drugs may not work for the long term and may have more resistance. Elo works well for most patients.

Q – Any studies on patients taking Revlimid for a long time? We are told to take Acyclovir for the rest of our lives. What could happen with that?

A – Certain drugs in certain classes have long term studies. There are patients on Acyclovir for 15 – 20 years and they are doing well. Revlimid has a risk of secondary cancers that needs to be weighed against keeping the MM away. Keep asking questions about your current drugs and alternatives as time passes. Research is constantly progressing.

Q – If Revlimid is maintenance for the long term, is the Dex still needed?

A – Most patients just take the Revlimid. As I have said at this meeting before, Dex is like bacon. It is great in small amounts, but in the long term it can create lots of problems, like impact on blood sugar and other issues.

Q – Should I switch to Pomalyst to avoid resistance?

A – If it is not broke, don't fix it. Stick with what works and keep the new drugs in reserve.

Q – If I have kidney issues, can I be on clinical trials? How does chemo affect kidneys?

A – I am interested in people with kidney problems. How do MM drugs work in people with kidney dysfunction? I am now writing a paper. Do patients with kidney problems have different side effects or the drugs don't work as well?

Q – I did not lose kidneys from MM. I went to a nephrologist and was told that I had chronic kidney disease. It is important for everyone to watch their creatinine levels. Would I be eligible for transplant?

A – Everyone should know the CRAB criteria and monitor their numbers and tests. Know all your drugs and ask about the effect on the kidneys. We transplant patients on dialysis looking at all side effects. Most people do well with transplant. Transplant is still a good treatment option.

Q – Should a patient consult a nephrologist about drug impact on the kidneys?

A – The oncologist will watch the creatinine levels and the patient should also watch and ask if they go up. Patients with a creatinine level of 2.0 or higher should ask questions to make sure their drugs are being dosed properly.

Q – Someone with kidney failure and on dialysis can take Velcade, but does Revlimid hurt kidneys?

A – Two questions on drugs and kidneys: Will the drug damage kidneys?; and What will happen? Revlimid will not hurt kidneys, but if the kidneys are not working well then there is more drugs in the body and you may need to reduce the dose. MM damages kidneys, so you may need 3 or 4 drugs to knock the MM down and the kidneys will recover.

Q – What if a person is on dialysis?

A – The first question is: how long? If only a short time for a newly diagnosed MM patient, it is not a problem. That is the time to be aggressive. If you have long term kidney problems, then you need to consider a different regime. Doctors don't want to do harm, but sometimes it is worth it to get the MM under control and reverse the kidney problems. That is where personalized medicine is appropriate, when it is based on all the patient issues and how the drugs will be tolerated.

Creatinine comes from creatine, a byproduct of muscle metabolism. Patients with a creatinine spike will get additional tests to determine if they are dehydrated. Elderly do not have a lot of muscle mass and could have a low creatinine level. Your healthcare team has to look beyond the numbers to other factors.

Comment: Jim has been on Revlimid for five years and said that he adjusts his life to the side effects in order to keep moving. His protein level is down to zero and feels he is blazing new trails.

Dr. Harvey said that they have to deal with a new side effect: Financial toxicity. A letter was published by Mayo and signed by Dr. Lonial and Dr. Curran (Director of Winship) and others stating that the current cost of new drugs to treat cancer is unsustainable. This applies to MM patients, especially in the combinations of new drugs that are each very expensive. Now, as patients are on maintenance with these drugs, the high costs continue for many years. Research and development are used as a justification for the costs, but the returns far exceed the investment. They are charging what the market will bear and the US gets the heaviest load. In Europe, they negotiate the amount and set prices. Sometimes this limits access to newer drugs and treats all patients the same. In the US, the drug costs increase every year and that approach is not sustainable.

Q – Don't MM patients have different markers? Can there be on drug for every patient?

A – We are finding new mechanisms that work for all patients where the markers do not matter. Everyone has T-cells, so the CAR T-cell immunotherapy uses the patient's own system to attack the cancer.

Q – Could you offer a final piece of advice to patients and families?

A – Always go to your primary oncologist if you have any issues, questions, or concerns. Also, an educated patient is an empowered patient who is also a better partner in healthcare. So keep learning!

Dr. Harvey welcomes questions and comments at Donald.Harvey@emory.edu

Business Issues:

The next meeting will be the Annual Luncheon, held at Atlanta's 57th Fighter Group Restaurant, located at the DeKalb-Peachtree Airport at 3829 Clairmont Rd., Atlanta, GA 30341. (770)234-0057.

August is our advocacy month. Members are encouraged to contact their Senator during the Congressional August recess to urge them to support H.R. 2739, the Cancer Drug Coverage Parity Act. More information on this issue, along with a form that you can use to contact your Senator, is available at <http://cqrcengage.com/myeloma/>.

New members:

One new member was in attendance. Marilyn's husband was diagnosed with MM in February 2015. He is in renal failure and is on dialysis. He is getting ready for a transplant in August.

Respectfully submitted by Nancy and Mindy

Southside Multiple Myeloma Support Group

Meeting Minutes August 2015

Doris opened the meeting with a moment of silence. There were 18 present; Josephine a guest of Doris visited with the group for the first time.

Old Business

Shop for a Cause tickets were still available, as a group we got 200 tickets/coupons from Macy's providing us with a potential of \$1,000 to be added to our treasury if sold.

Valerie and **Pat** attended the LLS Blood Cancer conference June; they reported that the conference offered excellent workshops on exercise and nutrition, informative topics regarding advances in the treatment of MM and other blood cancers. The conference was held at the Cobb Galleria; there were lots of door prizes and lunch was great. Pat shared that participants were encouraged to become active with advocacy to help ensure cancer medications are affordable. Cancer Community Support at Perimeter provides health and nutrition workshops, yoga, exercise classes and other workshops for cancer patients at no cost.

Speaker: Debra Thompson, RN, Hematology Oncology nurse with the Atlanta Veterans Administration and one of the nurse consultants to our support group arranged for **Sandra Francis Atkinson, RPh**, to be our speaker. She is an infusion pharmacist with the VA, working behind the scenes to ensure drugs and medications for patients are appropriately prepared. **Mrs. Atkinson** reviewed the various categories of MM drugs and provided insight on how drugs work, how they should be taken, side effects and what to do if a dosage is missed.

How do anticancer drugs work? All living things are made up of cells. Cancer cells and normal cells grow by cell division. Cancer is an uncontrolled growth of abnormal cells within the body. **Cytotoxic drugs** kill cancer cells by inhibiting cell division of fast growing cells. When cancer cells are unable to divide they die. **Targeted drugs** work by blocking the growth and spread of the cancer by interfering with specific molecules within the cells. **Hormonal** drugs work by causing the cancer cells to kill themselves.

Drugs taken in the treatment of myeloma include **Immunomodulator Drugs, Proteasome Inhibitors, Alkylating Agents, Corticosteroids, and Bisphosphonates** (used to strengthen bones).

Immunomodulator Drugs are classified as targeted cancer therapy. They primarily work by enhancing the body's natural immune system's ability to fight cancer. These include: Thalidomide, Pomalidomide and Lenalomide (Revlimid). Common side effects include drowsiness, fatigue, severe constipation, painful nerve damage, low platelets, low white blood cell counts. More serious side effects include Blood clots and liver problems. Talk to your doctor about these side effects.

Proteasome Inhibitors are also classified as targeted cancer therapy. They work by inhibiting the discharge of cell proteins which causes the cancer cells to die. These drugs include Bortezomib (Velcade) and Carfilzomb (Krpolis). These medications are injected and will always be given in a hospital or clinic setting. Drink plenty of fluids so you will urinate often to prevent kidney problems. Common side effects include tiredness, nausea/vomiting/diarrhea, and shortness of breath, fever, and low blood count. Velcade may cause nerve damage (tingling, numbness, pain in hands and feet. Note those using subcutaneously experience lower episodes of neuropathy. Patients on this medication may also be predispose patients to shingles (to prevent patients usually are prescribed Acyclovir—an anti-viral medication).

Alkylating Agents are classified as cytotoxic cancer therapy. They work by inhibiting cell division of fast growing cells. This may include destruction of other fast growing cells that grow hair. Medications included in this group are Cyclophosphamide (Cytosin) and Melphalan. Melphalan is used in high doses for stem cell transplant, but much lower doses are effective in controlling MM with fewer side effects. **Common side** effects include hair loss, mouth sores, loss of appetite, nausea/vomiting, low blood counts, and shortness of breath.

Corticosteroids are drugs classified as **hormonal** therapy drugs. They work by causing the cancer cells to kill themselves and used with other drugs to enhance effectiveness. These drugs treat inflammation and they also decrease nausea and vomiting. These drugs include dexamethasone and Prednisone. **Side effects** include high blood sugar, increased appetite and weight gain, problems sleeping, changes in mood (hyper). When taken for a long time these medications can suppress the immune system; this can lead to increased risk for infection and they can weaken bones. Most of these side effects go away over time after the drug is stopped.

New drugs: Panobinostat is a targeted drug that was approved by FDA in February of this year; it is a drug that can be used to treat patients who have already received at least two other treatment. **Side effects:** diarrhea, tiredness, nausea/vomiting, swelling in the arms and legs, decreased appetite, fever, weakness, drug may affect blood cell counts, and levels of certain minerals in the blood. More serious side effects include: severe diarrhea, cardiac arrhythmias, food interaction—avoid star fruit, grapefruit and pomegranate.

Ms. Atkinson said that although a single drug may be used to treat multiple myeloma, multiple drug combinations are used to more significantly reduce the Myeloma. The choice of drug therapy depends on many factors, including the stage of the cancer and kidney function of the patient. Be sure to read all instructions. Discuss new drugs and combinations with your doctor to understand the side effects.

Q: What is the pharmacist's role in Patient Centered Care? A: At the VA, the pharmacist meets with patients to go over medications – this is a policy as part of the **Affordable Care Act**. Debra said make sure you share with all pharmacies all medications, herbs and supplements you may be taking.

Q: What can be done ensure patients are able to actually get prescribed medications from the pharmacy, particularly narcotics, that are sometimes unavailable when needed? A: Debra suggested staying with one pharmacy, even introducing yourself to make them aware that you are a cancer patient and will need certain medications monthly. Also, you can speak with the provider and make him/her aware that you are having trouble obtaining the medication. **Debra** cautioned not to continue to take old medications. She shared that she had a patient whose doctor changed her blood pressure medication. The patient continued to take the old drugs plus the new ones because she did not want to waste medication she had previously purchased.

Announcements/Resources and Upcoming Events

- **Daratumumad-Janssen-J&J**-Expanded Access Program (EAS) for double refractory for both proteasome inhibitor and immunomodulatory drugs; 2-3 prior therapies. There are specific inclusion/exclusion criteria. Contact your doctor for more information.
- **Kyprolis (carfilzomib)**- FDA approved supplemental New Drug Application (sNDA) for injection in combination with Revlimid (lenomidomide) and Dexamethasone (KRd) for treatment of MM patients with 1-3 prior lines of therapy. Fills unmet need for released patients. Onyx/Amgen.
- Electronic Medical Records-**Debbie** Birns, Medical Editor. Importance of keeping personal copy of medical records. 8 – minute video. Go to www.myeloma.org click on IMF TV on red bar at top, and then select Myeloma Information to see the video.

Respectfully submitted by Paulette