MM Fighters! Support Group Meeting
May 1, 2021
Virtual Meeting

Dr. Bensinger appeared for his delayed but much anticipated discussion of his "Best of ASH" (American Society of Hematologists). He was greeted with an excellent turnout, including patients from across Washington State, California and Canada.

We want to thank the IMF (International Myeloma Foundation) for allowing us to continue to use their Zoom app for our support group meetings.

Thought For The Month

With all the challenges that we have faced due to Myeloma, COVID and curve balls that life throws us, do remember…

Wherever life plants you, bloom with grace.

Speaker
Dr. Bensinger from Swedish Cancer Institute was our presenter this month, discussing his yearly update on the **Best of ASH**. This year he combined information on the available Myeloma treatments with updates of the most promising new trials from ASH, creating an informative and easily understood presentation for all patients. The following is a summary of the slides to help guide you through them.

Dr. Bensinger began by outlining the frequently used treatments for Frontline therapy, as well as 2nd and 3rd line treatments (after patients relapse for the first and second time). While this was not an exhaustive list, and can vary depending on many factors, these treatments are what doctors usually reach for with most patients.

He then began showing how recent discoveries and clinical trials are changing such commonly held beliefs, demonstrating how the treatment landscape can change quickly. His first example was how quadruple therapies are starting to be considered frontline therapy due to the results of the **GRIFFIN trial**, where **RVD** was compared to **D-RVd** when combined with a Stem Cell Transplant (Revlimid, Velcade and Dexamethasone vs. Daratumumab-RVd). The 4 drug combination clearly showed a deeper and more sustained response vs. the triplet, although at the end of two years the PFS (Progression Free Survival) was approximately the same. However Dr. Bensinger feels that this will change as the follow up study continues. Dr. Bensinger has already started using this 4 drug regime when treating new patients.

Dr. Bensinger next turned to examine trials from several recent FDA approved treatments – **Isatuximab, Belantamab Mafodotin, Selinexor, Melflufen and Car-T cells**.

- The **ICARIA trial** compared **Pomalidomide – dex** vs. **Isatuximab – Pomalidomide-dex**. The triplet showed a much higher response rate (35% vs. 60%) along with an extended PFS (6.47 months vs. 11.5 months).

- **DREAMM2 trials** were then reviewed which featured **Belantamab Mafodotin,** a **BMCA targeted anti-body/drug conjugate**. BMCA is a highly expressed protein on Myeloma cells, making it a great target for drugs. **Blenrep** brings the drug to the cancer cell, binding with the tumor cell, which causes this drug to be absorbed into the cell, which then dies. The lower dose was found to be the most effective with the least toxicity, although the more heavily pre-treated patients did not respond quite as well. One side effect of this treatment is **Keratopathy,** an ocular problem that requires eye exams before each treatment.

- **Selanexor,** which is a **protein export inhibitor** was the next treatment examined (cancer cells require more protein than most cells, so by stopping export of protein to the nucleus of the cancer cell, the drug kills it). The **Boston trial** compared **Selanexor-Velcade-dex** vs. **Velcade (Bortezomib)-dex.** The Selinexor combo added 4.5 months to the PFS. The patients also experienced several side effects, including nausea, low sodium and appetite suppression, all of which as usually easily treated.

- **Melphlufen,** is a combination of **Melphalan and a protein**. This protein causes the drug combination to be more quickly taken into the cancer cell, where the bond between the protein and the Melphlan is broken, allowing the Melphlan to stay in the cell longer, killing it. The idea of combining a cancer killing drug with a protein is an idea that is starting to get tested with other combinations and shows great promise. The **Horizon trial** displayed that **Melphlufen-dex** was able to extend PFS for an extra 3-4 months .

Dr. Bensinger next turned to newer treatments, **Car-T cell therapies** (T cells modified to attach to and kill tumor cells) and **Bites (Bi-specific Anti-bodies**) (T cells combined with a tumor-binding agent).

There are a few differences between these two treatments:

Car-T cells only need to be given once, but patients must wait at least 4 weeks for this treatment to be created. **Bites**, on the other hand, are infused every 2-3 weeks, and are an "Off the Shelf" treatment – that is they are available quickly. Unfortunately, patients undergoing either treatment often experience **CRS**

(Cytokine Release Syndrome), the severity of which has lessened as the doctors have learned to treat it effectively. This tends to be less of a problem with Bites.

Although his slides featured summaries of 6 Car-T cell data, Dr. Bensinger only reviewed two:

- **KARMMA trial** – recently approved **CAR-T cell Ide-Cel** (Idecabtagene-vicleucel) had great results in this trial. Patients all responded within one month. The highest response rates were found to be the patients that who had the highest expression of cells. Unfortunately, at the one year follow up, they have found that most patients have had a much lower expression of Car-T cells, which points to a problem with the longevity of this treatment.

- There was also a study of the **Universal trial**, an **allogenic Car-T cell** treatment, with the T-cells coming from donors instead of the patient. There is less wait for this type of treatment as it is considered "Off the Shelf", as well as fewer episodes of GVH (Graph v. Host disease). Only a single infusion is required. There were 4 levels of treatment, with the highest dose being the most effective. However, this trial is still in very early days.

10 studies at ASH focused on **Bites**, and they found that those that are created with a larger molecule have longer durability. Dr. Bensinger briefly looked at the top 4 trials, focusing on two:

- the first in human trial of **AMG107** (**Pavurutamab**) and found that the response rate was 83%. Some very promising data, although this is still in the early stages.
- **REGN5458** also showed some impressive responses, with 95% of the 19 patients at VGPR or better (Very Good Partial Response).

Wrapping up his presentation, Dr. Bensinger reviewed two other novel treatments – Iberomide and Venetoclax.

Iberomide is the successor to Palmalidomide, but Dr. Bensinger is not certain that this will have much of an impact in the treatment of Myeloma. It was combined with different drugs (Daratumumab or Velcade or Carfilomib) in the trails reviewed.

Venetoclax, on the other hand, has been approved for several other cancers, but not yet for Myeloma. In the **Bellini trial,** (Venetoclax-Velcade dex vs. Velcade-dex) it was found that patients with the 11:14 translocation or that had high expression of BCL2 did well with this treatment, while those without either had much less success.

Dr. Bensinger's slides are attached to this email.

Patient Roundtable

We were able to meet several new members of the MM Fighters, including Nancy, Melva, and Noel, listening to the challenges that they are facing and providing insights and suggestions where appropriate. Welcome to the group!

Several members of the Stem Cell Transplant group were in attendance, including the new leads for the group, Michael and Erica. A lot of positive energy is flowing from the group, and Barbara, who just wrapped up her transplant, is now part of the Transplant Team. Anyone else who is considering a transplant, or is about to undergo one, please let the group know. Great support, information and insights!

The LLS is conducting a free study for blood cancer patients who want to discover if their Covid vaccines have produced anti-bodies. Please contact the Leukemia and Lymphoma Society, either online or via phone, for more details.

Susie, the head of the Myeloma support group in the Tri-Cities area, joined us this week. Working with a co-chair, Susie has put together a support group that hosts patients with several different blood cancers – quite impressive!

The Defeat Myeloma Walk/Run, a virtual event this year, is raising money for Myeloma research at the Fred Hutch, which benefits all Myeloma patients. The MM Fighters have set up our own "team" and if you would like to donate to this important cause, please visit https://runsignup.com/Fight-On

You can also donate to other teams or individuals, or create your own team. Registering for the race is free to all Myeloma patients (and you'll receive a nice race jersey), and $35 for all others. For more information visit www.defeatmyeloma.org.

Next MM Fighters! Meeting:

Saturday, May 22nd, 2021 – 10AM – Noon **Dr. Damian Green, UW/SCCA/Fred Hutch, CAR-T cels and Immunotherapy** – Virtual Meeting

Saturday, June 26th, 2021 – 10Am – Noon – **Dr. Avasare and Dr. Kwok – Myeloma and the Kidney** – Virtual Meeting

Sunday, June 27th 2021, **Defeat Myeloma Virtual Walk Run** – fundraiser to support myeloma research at Fred Hutch. Donate at https://runsignup.com/Fight-On

October 9th, 2021 – IMF Regional Workshop for Washington State – details will follow!