

MM Fighters! Support Group Meeting

May 22, 2021

Virtual Meeting

For the second month in a row, a much anticipated, but long delayed presenter was able to join the MM Fighters! **Dr. Green**, from the **UW/SCCA/Fred Hutch**, appeared to discuss **Immunotherapies** and the latest advances in this field. Uniquely positioned to discuss this exciting subject, Dr. Green is not only a leading researcher in this field, but also an educator, lecturer and practicing oncologist, which needless to say takes up an amazing portion of his time. We were very fortunate to have Dr. Green join us and share his knowledge.

We want to be sure to thank the IMF (International Myeloma Foundation) for allowing us to continue to use their Zoom app for our support group meetings. The IMF does a great job assisting support groups such as ours, and this is just one more example of their wide-ranging activities.

Thought For The Month

During our Myeloma journey, for patients it is easy to focus on ourselves and the many challenges we run across during our treatments. However, remember that

Life's most persistent and urgent question is, "What are you doing for others?"

By seeking to assist others, the focus shifts, and we tend to forget how we feel, thus helping relieve some of the worries, stress and strain. Such actions also help others feel better, which in turn makes us feel even better.

Speaker

Dr. Damian Green from the Fred Hutch, began his presentation with an introduction to **Car-T cell therapies** and how Car-T cells are “manufactured”:

- Car-T cell therapy is a repurposing of the body's immune system to attack a specific target.
- For Myeloma treatments, this target is the Myeloma cells, or more specifically, unique targets (proteins) on the surface of the Myeloma cell.
- There are 4 characteristics of a good target
 - o Unique protein on the cell of Myeloma cells only
 - o Stable (does not fall off, or is not shed into the blood stream)
 - o Dense (A lot of expression on the surface of the cell)
 - o Stays on the surface (does not get absorbed into the cell)
- In addition to common targets used by researchers (BMCA, SLAMF7, etc.) promising new targets are now being researched (FCRH5 and CPRC5D).

The first FDA approved Car-T cell therapy for treatment of Multiple Myeloma is called **Idecabtagene-Vicleucel**, or preferably, **Ide-cel**.

- Between all the studies done, overall responses have been very good, between 70-80% of patients.
- Complete response has been around 40%.
- Duration of responses have been approximately 1 year.
- Unfortunately, cytokine release syndrome has occurred in 96% of patients.
- There also have been cases of neurotoxicity.

In another promising clinical trial, the Cartitude trial, Jassen's Car-T cell therapy **JNJ-4528**, has shown good promise, perhaps even a bit better than Ide-cel.

- Overall response rate of this early trial was 96%
- Patients are still relapsing....

Fred Hutch Car-T cell trials are a bit different than others out there...

- Currently 6 ongoing Myeloma related Car-T cell trials at Fred Hutch/SCCA.
- While targeting BCMA, the trails at Fred Hutch/SCCA select different proportions of various Car-T cells in order to create what they feel is the most effective combination (few other trials do this)
- Gamma Secretase Inhibitor (**CSI**) is given to patients before the Car-T cells in order to bind the BCMA to the myeloma cell, thus eliminating most of the "decoy" BCMA floating in the blood stream and marrow.
- This addition also seems to boost the total amount of BCMA on the myeloma cells greatly, making them much more "target rich".
- At the lowest dose, the amount of BCMA increased 32 fold, and after 31 months still no relapse.
- In a 2nd patient, at a higher dose, the BMCA increase by 157 fold, but the patient relapsed after 18 months.
- This shows the difference between patients and that there is still much work to be done in order to keep Car-T cells active longer.

BiTE (Bi-specific T cell Engager) – targets two points, one on the surface of the Myeloma cell and the other on a T cell, thus bringing the two into contact so the T cell can kill the Myeloma.

- The advantage of this treatment is that it is off the shelf, ready quickly for patients in need.
- Instead of one dose as with the Car-T cells, there are frequent doses required in order to be effective.
- A high response rate has been found in trials up to this point, but cytokine release syndrome still occurs.
- Amgen, who seems to be leading in this area of research, is modifying their product in order for it to remain active for longer periods of time.

One of the new protein targets on the surface of Myeloma cells, **GPRC5D**, is also found on skin cells. However, clinical trials have yet to find any related toxicity (yet!).

- **Talquetamab**, which is a BiTE that binds to GPRC5D on the Myeloma and CD3 on T cells, has shown to have a 73% response rate in its initial trial.

Anti-Body Drug Conjugate (ADC) Blenrep (belantamab mafodotin) delivers an drug killing “package” to specific proteins (in this case BCMA) on the Myeloma cell surface in order to kill the Myeloma.

- Unfortunately, this toxin also causes vision problems.
- There are investigations into whether introducing a Gamma Secretase Inhibitor would help, as it would increase the expression of the BCMA, which would then require less ADC to treat the Myeloma, possibly lessening the vision problems.

Work is ongoing with the Allen Institute and SCCA to follow the immune function in MM patients.

Also working in conjunction with the LLS and Emory on Car-T cell investigation comparing the hourly increase in death rate of MM cells when using a Gamma Secretase Inhibitor as part of the treatment.

Dr. Green’s slides will be sent along at a later date, once they are available.

Patient Roundtable

A lot of discussion around neuropathy and ways that patients handle it. Some of the suggestions put forth by the group include

- Plenty of walking (at least 30 minutes a day)
- Foot massages
- Vitamins B6/B12 (be careful of the dosage!)
- Acupuncture
- Soaking in warm water and Epson salts
- Physical therapy – specific exercises to address this issue
- Gabapentin

As with all treatments, discuss these with your oncologist/hematologist first!

More MM Fighters are undergoing stem cell transplants – our best to all for a quick recovery of their immune systems....and hair!

Melva has been in the hospital due to the sudden development of blood clots. Hope that she is able to return home soon.

Bill joined us, and let us know that his hospice care has been a great help with his pain, and that his sense of humor is still firing on all cylinders!

Dave in CA has hopefully found a solution to the back and leg pain that has been plaguing him. He is very pleased with the support from City of Hope.

And leading the way for others....

Ruth is doing well with her clinical trial, which is great news.

Anne is now taking Venetoclax in combination with Carfilzomib and Dex instead of solo, hoping for better results.

The Defeat Myeloma Walk/Run, a virtual event this year, is raising money for Myeloma research by **Dr. Green** 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.

So far there is over \$2,500 donated by the MM Fighters and their relatives, with tens of thousands of dollars raised by other MM Fighters starting their own teams. Thank you all! Still one month to donate!

Next MM Fighters! 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!