AA·MDS INTERNATIONAL FOUNDATION

35 YEARS

MDS Update

Connecting Patients and Families with News and Expert Opinion

INTERVIEWS WITH THE EXPERTS

VOLUME 8, NUMBER 3, NOVEMBER 2018

The MDS Clinical Research Consortium

The MDS Clinical Research Consortium (MDS-CRC) is an unprecedented, six-institution group designed to undertake unique studies and trials to advance treatments and improve outcomes for patients with myelodysplastic syndromes (MDS). Member institutions are six academic medical centers serving a high volume of MDS patients:

- Cleveland Clinic Taussig Cancer Institute
- Dana-Farber Cancer Institute
- H. Lee Moffitt Cancer Center and Research Institute
- MD Anderson Cancer Center
- Weill Medical College of Cornell University
- Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

The consortium is co-chaired by Amy DeZern, MD, MHS at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, who provides oversight and direction for all scientific matters. Here, Dr. DeZern speaks about the MDS-CRC and effect it has had on specific research that might not have been published as quickly if it not been conducted by the MDS-CRC.

Q What is it about the concept and function of the MDS-CRC that makes it a unique enhancement to traditional MDS research?

A This is the first endeavor of its kind in the United States – it's a wonderful, collaborative effort between six large MDS programs to run trials together in a more efficient way and hopefully bring new drugs to patients sooner.

Q Are there any MDS-CRC studies that would not have been possible without the wider scope that MDS-CRC participation allows?

A There are two good examples of this. One is a research study on CMML, a rare MDS/MPD overlap disease. Because it's an unusual patient population given the disease rarity, having the consortium, in addition to Moffitt as the lead site, to more quickly accrue enough patients for this study was very helpful.

Amy DeZern, M.D.S., Mph

Dr. Amy DeZern is a hematologist and medical oncologist at the Sidney Kimmel Comprehensive Cancer Center and is an Associate Professor of Oncology and Medicine at the Johns Hopkins University School of Medicine.

Dr. DeZern's primary clinical and research interests are focused on bone marrow failure disorders. She has expertise in the diagnosis and treatment of myelodysplastic syndromes (MDS), aplastic anemia (AA), paroxysmal nocturnal hemoglobinuria (PNH), and other bone marrow failure syndromes as well as acute leukemias.

A second example is a randomized trial, headed by MD Anderson, of two approved MDS drugs in decreased dose or schedule, azacitidine (Vidaza®) and decitabine (Dacogen®) which are already used in practice at higher doses. Outside the consortium environment this study would not have been possible through more traditional avenues. This trial is going well with good accrual and I think we'll have some great results for the field in the near term.

One other thing to keep in mind is clinical trials have a lot of regulatory aspects –they are paperwork intensive, and not an altogether efficient process, besides all the aspects of patient care. So, having several centers working in coordination can be helpful.

continued on p. 2 ▶

continued from cover

The MDS Clinical Research Consortium

Q Are there any MDS-CRC studies you have a particular interest in?

A Yes, currently there is a study specifically targeting a high-risk form of MDS—those with TP53 mutations which carries a very poor prognosis. There's a currently Phase I/II trial, led by Moffit Cancer Center, that the MDS-CRC sites are participating in that is accruing well. It's an exciting time in MDS right now and we hope to make progress with a new drug for this high-risk MDS subtype.

Q Do the participating centers have different roles in the MDS-CRC or are they all the same kind or level of participation? Does data sharing play a role?

A It's generally the same participation by all centers, though the patient volumes vary some by region – but the experience of planning and running the trials is pretty much the same. Data sharing has been useful to have a larger aggregate group to examine results and statistics from. There have been some successful abstracts that benefitted from having this larger pool of rare disease data.

Q The MDS-CRC is an example of a partnership that combines resources to increase the pace and scope of research. Is this working out as you had hoped and are there any 'next steps' for the MDS-CRC?

A Overall it is working very well, and we have been very productive as group since the inception of the MDS-CRC. We are currently exploring all ways possible to maintain the funding to continue this endeavor for years to come.

Two MDS Clinical Research Consortium Studies

Promising Results of a Phase 1/2 Clinical Trial of Ruxolitinib in Patients with Chronic Myelomonocytic Leukemia

MDS/MPN (myelodysplastic syndromes/ myeloproliferative neoplasms) is a disease of the blood and bone marrow with features of both MDS and MPN. The most common form is CMML, or chronic myelomonocitic leukemia. In CMML, abnormal blood cells (myeloblasts and myelocytes) accumulate in the bone marrow and other organs, and they interfere with the production of healthy blood cells. This study led by Dr. Eric Padron through the MDS Clinical Research Consortium sites showed promising results for a new CMML treatment.

This Phase I/II study was conducted by Dr. Eric Padron of the H. Lee Moffitt Cancer Center between April 2015 and October 2016. It was done to test the efficiency of ruxolitinib, known as a JAK1/2 inhibitor, for treating CMMLAccording to Dr. Padron and colleagues, the outcome of the Phase II study is encouraging. In results published in the journal Blood they concluded, "ruxolitinib has promising activity in CMML patients with particular benefit in those with proliferative symptoms and may have disease-modifying activity." Further clinical study is needed to validate the biomarkers of response and effectiveness of ruxolitinib in CMML.

For more information, please visit www.bloodjournal.org/content/128/22/343

Phase 1/2 Study of AG-221 in Subjects With Advanced Hematologic Malignancies With an IDH2 Mutation

This multicenter study, which began in 2013, was led by Dr. Eytan Stein at Memorial Sloan Kettering Cancer Center in New York, NY. Its purpose was to evaluate the safety and efficacy of orally administered AG-221 (Enasidenib) in subjects with advanced Acute Myeloid Leukemia (AML) that harbor an IDH2 mutation. As a result of this phase I/II study, and Celgene's request for priority review status, the FDA approved of AG-221 in August, 2017 for patients with relapse and/or refractory AML with an IDH2 mutation.

During the study, researchers discovered that AG-221 also had a positive effect on MDS patients with an IDH2 mutation. This discovery led to a clinical trial involving AG-221 for the treatment of MDS with an IDH2 mutation, which is currently being led by Dr. Courtney DiNardo and Dr. Guillermo Garcia-Manero at MD Anderson in Houston, TX. Drs. DiNardo and Garcia-Manero were able to secure the assistance of the MDS Clinical Research Consortium and expand the trial to the CRC's six participating institutions. This allows the research team to collaborate and share resources, and it expedites the study's timeline. Successful completion of this trial could eventually lead to an FDA approval of AG-221 for patients with MDS who have an IDH2 mutation.

For more information, please visit www.bloodjournal.org/content/130/Suppl_1/162?sso-checked=true

PATIENT STORY

Ron Carlsen Beats Early Onset MDS; Grapples with Post-Transplant GVHD

Ron Carlsen

In August 2004, I was 42 and going through the annual checkup routine. I felt fine and had no reason to suspect anything was starting to go wrong. I was called back twice to have more labs done. My doctor wouldn't speculate on what might be happening, but soon I was referred to a hematologist/oncologist. This is when a bone marrow biopsy was done and it confirmed that I had MDS, with the 5q deletion. There were no real changes in how I was feeling but they stated I currently could expect to live another 12 to 20 years, without a bone marrow transplant, but a bone marrow transplant was expected to eventually occur.

Low Risk MDS Quickly Becomes High Risk

Things changed quickly. I started to bruise easily with no explanation, and my red blood cell count started to drop. Eventually, I was put on epoetin alfa (Procrit°), taken by injection. My counts continued to drop and I became increasingly fatigued, and it became necessary to try another treatment.

Fortunately, azacitidine (Vidaza°) had recently been FDA-approved and was clearly another option to investigate. My treatment with this new drug was another injection in the stomach, like epoetin alfa was.

Azacitidine caused nausea, and I was given a number of anti-nausea treatments. It only worked a short while and my counts continued to drop. I was switched over to lenalidomide (Revlimid°), also recently FDA-approved, and was tapered off azacytidine before starting lenalidomide.

From diagnosis in August 2004 to October 2006, (just two short years), three trial drug treatments were tried, epoetin alfa, azacytidine, and lastly, lenalidomide. By October 2006, I had become blood transfusion dependent, requiring one each week. The new problem was my platelets which had dropped to almost nothing.

In October 2006, not happy with these results, my primary hematologist/oncologist sent me back to University of Wisconsin (UW) Hospital Cancer Center in Madison Wisconsin for a second consultation. My UW hematologist/oncologist recommended we do a transplant as soon as possible. He stated that without a transplant I had maybe 1 ½-2 years left. My platelet count was very low and would cause me to hemorrhage.

Shortly after diagnosis my siblings were tested to see if one was a match for a transplant, to prepare for the day one was needed. None of my siblings was a match and when it became time to find a donor, we knew that a transplant from an immediate relative was not possible. Through the national marrow registry, a complete match was found; my match was a woman in Germany. On March 9, 2007 the stem cell transplant occurred with no immediate complications however a long road of chronic GVHD followed post transplant.

With MDS Under Control, Ron Faces a New Health Challenge

My chronic graft-versus-host disease (GVHD) started after the transplant, first in the most common ways; skin and gut, and with time the flare-ups were more severe, resulting in frequent hospitalizations. One GVHD episode left me unable to eat anything. My weight dropped less than my high school weight. I was hospitalized and learned I had gastroparesis, a temporary paralysis of stomach function. For 2 ½ weeks I had a 12-hour intravenous, from nutrition bags – this is known as total parenteral nutrition (TPN). Other GVHD related issues that I faced were pneumonia, and GVHD of the lungs.

I have taken prednisone (a steroid) for nearly 12 years, to control GVHD. When I have a flare-up my prednisone dosage gets increased until it passes, then I resume my maintenance dosage. Prolonged prednisone use can be harmful and cause problems. Avascular necrosis (AVN), a deuteriation of joint tissue from loss of blood flow is one problem. I now have AVN, and have had both hips and partial shoulder replaced. Currently my eyes and mouth are the only places my GVHD fights me. An attempt to replace my prednisone with a safer medication is being evaluated.

We have met my donor and talk occasionally. On my 10th anniversary of the transplant, we Skyped with her family.

To others facing MDS, learn as much as you can about the disease, the treatments, the human body and your body. Become familiar with your body and always pay attention. Pay attention to all labs and treatments and always speak up.

Today I do as much as I can to help others with MDS, including working at marrow drives. In 2009, I worked 10 of these, including one my family hosted. That drive generated 150 registrants and saved one life!

My wife and I have been married for 36 years. We have two daughters, 32 and 29. In closing, always be as positive and upbeat as you can – this goes a long way. You are not alone, and don't be overwhelmed by little things.

AA·MDS
35 YEARS
INTERNATIONAL FOUNDATION

4330 East West Highway | Suite 230 | Bethesda, MD 20814

Learning is Hope, Connecting is Strength

AAMDSIF - Your best resource for medical and personal perspectives on myelodysplastic syndromes (MDS)

IN PRINT

Patient Guides*

- *Your Guide to Understanding MDS*
- *Your Guide to Understanding Clinical Trials*
- *Your Guide to Understanding Bone Marrow and Stem Cell Transplantation*

* Also available in Spanish

To order a patient packet, call (301) 279 7202, or order online at www.aamds.org/info

facebook.com/aamds
youtube.com/aamdsif
twitter.com/aamdsif
@aamdsif

ONLINE

Online Academy (www.aamds.org/learn)

- Live and Archived Webinars
- Interviews with the Experts
- Prerecorded Webcasts
- Interactive Learning Modules

IN PERSON

Phone Support for Personal Attention

Contact our patient educator at (800) 747-2820, option 2, or email help@aamds.org for answers on a wide range of subjects, including treatment options, clinical trials, financial resources and more.

Peer Support Network

Our Peer Support Network is a national group of trained volunteers, offering information, guidance and coping strategies from a personal perspective. To connect with a Peer Support Network volunteer, call (800) 747-2820, option 2, and speak with our information specialist who will match you with one of our volunteers. You can also email help@aamds.org.