

INTERVIEWS WITH THE EXPERTS

MDS Clinical Trials I'm Following

New uses for an existing drug

At this scientific symposium we're attending, results from recent clinical trials are being presented along with descriptions of upcoming trials, all of which I find very interesting. One of the recently finished trials highlighted at this meeting was a Phase 3 trial of an approved drug, lenalidomide that is principally used in patients with the del(5q) chromosomal abnormality (a missing piece of chromosome 5). Lenalidomide was originally found to be very effective in del(5q) MDS patients, but we now know that non-del(5q) patients can respond to the drug as well – although not at the rate that the del(5q) patients do.

But this large Phase 3 trial really proved that there are patients who can benefit from this treatment. About 27% of patients became transfusion independent and on average maintained that response for several months – in short, it had demonstrated a real clinical benefit. Therapy with lenalidomide for non-del(5q) patients has been available for some time but hasn't formally been part of the standard of care. But now with these new results, we can feel confident there will be a subset of non-del(5q) patients who can benefit. It's an incremental advance but still an important one.

The next therapy I'm excited about also looks at lower-risk MDS patients who are transfusion dependent. This therapy, that has recently completed phase 2 clinical trials, is for a drug called luspatercept. It is now moving into Phase 3 clinical trials in the U.S. and Europe, and I'm involved in this trial as part of the data safety monitoring committee.

Investigating a new drug

Luspatercept is exciting because it works in a completely novel way to help stimulate the production of red blood cells and to alleviate anemia. The earlier Phase 2 trials were encouraging because patients had strong responses that seemed to last as long as the drug was being given. So this suggests luspatercept may be a very good drug in the future for helping fight the anemias common to many patients with MDS. Part of this is figuring out who the best responders will be for luspatercept. For the Phase 3 follow-up, the focus is on a population of patients we think are most likely to respond – patients with the ring sideroblast subtype of MDS who appeared to have the best responses in the earlier Phase 2 trials. This will be an interesting trial to follow!

A new paradigm for treatment

There is a new drug that has not yet been tested in patients that I expect is going to be in clinical trials later this year. I'm not involved in the trial, but have followed the studies leading up to the drug's development. This will be a first-in-class splicing inhibitor that targets a molecular pathway we only learned about in the last 6 years.

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Rafael Bejar, MD, PhD
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Dr. Rafael Bejar is assistant professor of medicine in the division of hematology/oncology at University of California, San Diego. At the recent 2016 AAMDSIF Scientific Symposium, Dr. Bejar spoke to the *MDS Update* about clinical trials that he thinks are significant and show promise for advancing new MDS treatments.



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A subset of patients with MDS – just over half – will have acquired a mutation in a splicing factor. We think that the abnormal cells in these patients might be more susceptible to drugs that target RNA splicing and this trial will begin to test that hypothesis. Right now, it will be an early phase trial focusing just on safety, but the fact that it represents a totally new paradigm for MDS therapy is very exciting. In fact one of the pre-clinical studies indicating that this might be good therapy was one of the top abstracts presented at the ASH Annual Meeting in 2015.

Two proposed combination therapies fail to meet expectations

It does happen – there are trials I had high hopes for that didn't go well. A recent trial initially reported at the ASH Annual Meeting in 2014 and updated at the 2015 meeting examined combination therapies with existing, approved drugs. This was a large intergroup trial, open at various treatment centers around the country.

It tested two combinations of currently approved drugs – azacitidine with lenalidomide, and then azacitidine with vorinostat, to see if either of these combinations might be

better than azacitidine treatment alone. All of these drugs are FDA-approved, so had there been an improved outcome with either of these combinations, they would not have had to go through the approval process before hitting the market. These combination therapies would have been available to patients almost immediately.

We had hoped that the combinations would be safe, more effective and have no greater toxicity than azacitidine alone. But unfortunately, the results of the trial did not show that patients treated with azacitidine alone and those randomized to receive azacitidine and either lenalidomide or vorinostat were much different. The bottom line was that these combination therapies didn't have enough of a benefit to be worth the added toxicity we often saw in patients who received it.

Help advance research by participating

Clinical trials are the way we learn about what works to treat MDS and are how we bring new therapies into use. They are the best way for patients to try new - and potentially better - treatments early. I encourage patients with any type of MDS, at any stage, to consider participating in a clinical trial. ■

MDS Patients Sought for Research Study



CRUSH!!MDS (www.crushmds.org), is a research initiative at Weill Cornell Medicine, a member of the MDS Clinical Research Consortium (MDS CRC). One study is now in the process of recruiting patients who have not responded or lost their initial response to azacitidine or decitabine. Azacitidine (Vidaza®) and decitabine (Dacogen®) are FDA-approved drugs for the treatment of MDS. While these drugs help many patients with MDS, sometimes they stop working for patients who initially responded well to them. The study's investigators are trying to find out why this happens.

How do I know if I qualify for the study?

All MDS patients must meet these basic criteria:

1. Be at least 18 years of age with pathologically confirmed MDS
2. Must have received at least 4 cycles of decitabine-based or 6 cycles of azacitidine-based therapy and are either refractory to, relapsed after or intolerant to prior therapy with either agent.

If you think you're eligible, please review the informed consent form and record any questions you might have for the study team. After reviewing the informed consent form, please complete and submit the study questionnaire.

For more information, please contact Nicole Rizzo at Weill Cornell Medical College: nir2017@med.cornell.edu, (212) 746-1534. ■

The banner features a dark background with a white and red graphic of a hand holding a pill. The text is white and red, providing details about the 2016 Patient & Family Conferences. The registration information is presented in a grid format with dates and locations. The website URL is prominently displayed in red, and a note about free registration is included at the bottom.

Living with Aplastic Anemia, MDS or PNH
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registernow ▶

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www.aamds.org/conferences

Registration is FREE, but space is limited. Don't wait, reserve your space now!

* different format ** en español e Inglés

PATIENT STORY

Donna Adams - My MDS Diagnosis and Treatment Progression

I am 66 years old. I grew up in Massachusetts and New Hampshire, where most of my family still lives. I have been retired from the federal government for 6 years. My husband Jack and I moved to Pennsylvania from Northern Virginia when we both retired. My husband and I have 3 children and 4 grandkids. Jack's kids reside in Virginia and my son lives in Massachusetts.

I was diagnosed with myelodysplastic syndrome (MDS) and essential thrombocytopenia (ET) in July of 2013. In the summer of 2012, I started getting a burning feeling in my left foot. Because it wasn't that bad I let it go, but by the holidays of that year, I could barely put my foot down on the ground. I also noticed that my toes on that foot were turning blue. I made an appointment with a foot doctor who diagnosed me with Reynauds' Syndrome.

After 4 months of various treatments, none of which helped, he told me to see my family doctor. First thing was lab work, which showed a high platelet count. Within a few days, I was sent to a hematologist. More lab work was done and a bone marrow biopsy (BMB) was also completed. I was diagnosed with MDS, RARS-T classification. Fortunately, I did not have any chromosome damage or related issues, and still have none after a more recent BMB in August, 2015.

I was started on hydroxurea (Hydrea®) and darbepoietin (Aranesp®). I had the injections off and on until March of 2015 when it was decided that these were no longer working. After attending the AAMDSIF conference in Baltimore that same year, my husband and I decided to seek a second opinion from Johns Hopkins. They confirmed



the diagnosis and thought a different approach should be tried. My local oncologist and the doctor at Johns Hopkins decided to try ruxolitinib (Jakafi®), and stop hydroxurea.

Within weeks my platelets had risen to the 800's. My local oncologist restarted the hydroxurea and by mid-June ruxolitinib was stopped. I have since continued with various dosages of hydroxurea. I was able to stop all medication for a month when the platelet count was stable. Johns Hopkins is now managing my cancer care with the assistance of the local oncologist. I had 2 blood transfusions, in June and October.

Currently, I am experiencing exhaustion, some shortness of breath and lack of appetite. I'm sure it is both medication side effects and anemia.

I have been told that I may need to go to a more aggressive chemotherapy. I have 2 sisters who had breast cancer and have now cleared the 5-year mark, a brother who is being treated for chronic lymphocytic leukemia (CLL) and my dad passed from multiple cancers. I know what each has gone through during treatments.

There have been side trips on this journey, some encouraging, and some discouraging and not so pleasant. Until you have the experience, you don't understand the obstacles you have to surmount. My journey is with MDS, and I will somehow continue. ■

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I am hopeful about..

Living well and dancing with my grandchild's wedding
we're here for each other
growing old together

We Do This Work for You...

... because YOU are one of the many patients and families who count on us for support. We want to continue providing the best resources available, including MDS education and the latest research news, to help you find the treatments you need. We know that one day, a cure for MDS will be found but, until then, your donations make our work possible. The picture on the left is part of an actual banner we displayed at a recent Patient and Family Conference to show how patients feel about themselves and our community, which we've been serving for over 33 years.

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