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MDS Update

Connecting Patients and Families with News and Expert Opinion

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Computers and MDS: What's Here and What's Coming

Besides their presence in many routine aspects of 21st century life, computers have had a huge impact on medical research and treatment. Here, Dr. Christopher Cogle addresses how computers are being used to inform MDS research and treatment decisions.

Q Was there a progression of events leading to computers being used in MDS?

A Our understanding of MDS and other cancers has dramatically changed over the last few years in that we now recognize these disease as multi-genetic, clonal, and capable of evolution with time and in response to treatment.

This new appreciation of MDS comes from our ability to read its DNA. Current clinical practice and medical research is at the early step of asking what single gene mutations mean in terms of prognosis for survival and predicted drug response. However, when we look at the entire spread of DNA within MDS and other cancers, we find hundreds of genomic abnormalities. It is impossible for the human brain to understand this level of complexity.

To fully interpret the panoply of gene mutations and the millions of possible interactions among them, we have to use computational approaches. We're in an exciting era of medical history when both DNA sequencing and computer engineering are advanced enough to help each other.

My group developed a computational biology method of creating computer models of our patients' MDS, myelofibrosis (MF) or acute myeloid leukemia (AML) cells by inputting their unique constellation of genomic abnormalities. The computer model shows us which intercellular networks are disturbed. The computer model also allows us to digitally simulate drug treatments and digitally screen for drugs with high efficacy in reducing cancer cell growth. In essence, we're performing multi-gene, multi-drug matching using the patient's specific gene mutation.

Q Is there an area in which computers are thought to be of particular help?

A The MDS grandparent of computational algorithms is the IPSS. It has been and will remain important because it continues to be updated and revised by new research findings. However, in its current form, it is limited by its simplistic categorization of genetic and cytogenetic abnormalities. Certain gene mutation or chromosome abnormalities may have prognostic impact of their own (also called independent prognostic indicators), but their impact can be influenced by additional and secondary gene mutations.

We'll see this algorithm continue to evolve and remain relevant to MDS because the MDS community believes we need to have a universally accepted method of quantifying the disease. My prediction is that the future IPSS will have to treat the patient's cytogenetic, genetic, epigenetic, and RNA spliceotypes with much more sophisticated calculators.

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Christopher Cogle, MD

Associate Professor of Medicine

University of Florida

Dr. Christopher Cogle is a professor of medicine at the University of Florida, Gainesville, Florida. He has clinical and research expertise in myelodysplastic syndromes (MDS), acute myeloid leukemia (AML), and allogeneic hematopoietic cell transplant. Dr. Cogle leads a clinical and laboratory research group that translates fundamental scientific discoveries into new treatments and diagnostics for patients.

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Where there's an opportunity for computers is in appreciating that every MDS patient is different from another. There's a highly unique constellation of gene mutations in every genetic and splicing abnormality that are specific to the patient and his or her MDS clones. Herein lies the opportunity for clinicians to use computers to better understand the disease, better prognosticate disease progression and survival time, better predict response to treatment, and search for tailored therapies that match the patient's specific disease biology.

Q What are some of your studies in this area?

A After 10 years of diagnosing and treating MDS patients, I was extremely frustrated by the 40-50% success rate in improving clinical outcomes with available drug therapies. I saw the hundreds of genomic abnormalities, but was stymied in how to interpret that complexity. After meeting with several bioinformatics specialists and systems biology experts, I finally found a software engineering company that could create what my patients needed: a computational biology method of simultaneously mapping hundreds of genomic abnormalities and simulate drug treatments, all within seconds.

I hired Dr. Leylah Drusbsoky, an outstanding young scientist, to lead this effort. She and I created a precision oncology program called iCare for Cancer Patients at the UF Health Cancer Center, which tested the feasibility of computational oncology in patients with MDS and other blood cancers. Dr. Drusbosky has 14 presentations at ASH 2017, showing high accuracy in predicting treatment response and identifying new drug combinations for patients with MDS, AML and multiple myeloma.

Q What is your next step?

A Our next step is to test the extent by which computer-informed treatment improves clinical outcomes compared to standard of care. In the first quarter of 2018, Dr. Drusbosky and I are initiating a phase 2 clinical trial in patients with relapsed or refractory MDS who will be randomized to either computer-informed treatment or standard of care. We expect to find a greater proportion of MDS patients receiving computer-informed treatment will have achieve improved response to tailored treatment.

Q What do patients need to know about computers and MDS, relative to their own treatment?

A Today, computers are used to keep track of each patient's gene mutations, but it is still up to the treating physician to remember the significance of the gene mutation, its impact on treatment decision, and how to monitor for genetic response. Using a computer to aid the treating physician is still experimental. At this point, we can say that computers are on trial. I first advise patients to make sure they have their chromosomal and genetic testing reports and results. Genetic test results are powerfully prognostic and can be predictive of drug response.

In the focus groups that I've conducted with MDS patients, I find that most patients want to know what genetic mutations they have. But they have to rely on their doctors to explain the results. Unfortunately, many physicians simply don't have the time to study the significance of the chromosome or genetic abnormalities.

My group foresees patients getting caught between a treating physician's lack of time and the new appreciation of MDS genomic complexity. Our goal is to aid the physician and patient in rapidly understanding the MDS biology and tying it into sound treatment decisions. Ultimately, we see a day when patients live longer because of tailored and re-tailored treatments for MDS.

Q What does the future hold for computers in MDS?

A We're already working on the next big opportunity for computers in MDS. Dr. Drusbosky and I have developed a method of serially monitoring MDS disease burden with specific measurement of multiple MDS clones and clonal evolution within individual patients. We believe that if treating physicians can see the clonal dynamics of the MDS clones in response to treatments, they will have a much greater grasp on the enemy that they're trying to eliminate.

In this effort, computers are necessary to read genomic data and draw the clones over time. We have a vision that treating physicians will one day stand before a screen that shows the comings and goings of clones with respect to treatments, and that the latest clones will be presented with a description of predicted treatments with low chance for efficacy and predicted treatments with high chance for efficacy.

As a professor, I feel like the computer is one of my medical students. The benefit is that my computer-student has perfect memory. But, as I teach my students, whereas cancer can be calculated, cancer care is never completely calculable. Listening to patients and authentically being present with them matters as much as making the right calculation. ■

PATIENT STORY

Vincent Tackles MDS with Information, Treatment and Personal Support

Vincent Rusak

Vincent Rusak of New Kensington, PA, traveled extensively during his 26-year career as an expert electronic service technician. For 15 of those years, he was also a regular blood donor in his community. His father's quadruple bypass surgery, as well as a deep compassion for his fellow man, were Vince's motivation for contributing to his local blood banks every six to nine months. Little did he know that this selfless habit would someday save his life.

One day 13 years ago, Vince went to give blood as usual. "But when they pricked my finger and put the blood drop in that liquid, it was supposed to sink, but mine floated," he said. "They thought it was because I had no iron, that I was iron deficient." The extensive blood work that followed told a different story. Vince never had any of the symptoms typically associated with bone marrow failure disease, so his MDS diagnosis came as a serious shock.

He clearly remembers being terrified when he heard how short his life expectancy would be, but that's because his doctor at the time had left out a crucial detail – if he decided against getting treatment, the result would be a dramatically abbreviated life. He wasn't going to let that happen. Like so many patients, Vince initially struggled with depression. But as soon as he pulled out of it, he went online in search of information.

Vince's doctors tried a variety of treatments over the years. While some were beneficial, others didn't work. Positive results came when his doctor began treating him with lenalidomide (Revlimid®) on and off for five years. Whenever his blood counts looked good, the treatment was stopped, but Vince occasionally still needed blood transfusions.

More recently, his blood counts dropped yet again, so in addition to increasing his transfusions, he started taking a different drug this year.

Even though he tires easily, Vince is now doing well on azacitidine (Vidaza®) and is able to keep up with his favorite activities.

He became involved in an MDS forum that introduced him to AAMDSIF, and that, he says, was a game-changer. "I learned so much at those patient and family conferences, from the caregivers and other patients and from the wonderful medical experts who speak there. Everyone should go to at least a couple of these conferences," Vince states. That's where he learned about the importance of self-advocacy, including how to find the right doctor and prepare for his appointments with his health care team.

Vince has several layers of support, but the first person he turned to when he was diagnosed with MDS was his youngest daughter Jade, whose own little girl is now the center of their attention. Jade is still a pillar of support for her father. Since she lives nearby, she also keeps dad beaming and busy helping her care for her toddler. As a 13-year survivor, Vincent believes that in addition to family, he's had several distinct advantages in learning how to cope with his chronic disease – the support of the Foundation, the constant companionship of his beloved pets and his abiding faith in God.

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