Making the tough calls on cancer drugs

Maha Hussain, MD (below), knows a lot about cancer. She also knows a lot about the intricate details of carrying out clinical trials of new treatments, and analyzing the data that they generate. And every day, she uses that knowledge as a genitourinary cancer specialist and researcher at the U-M Comprehensive Cancer Center, and in her role as chair of the U.S. Food & Drug Administration’s Oncology Drugs Advisory Committee.

But when that committee is reviewing a new cancer drug, and deciding whether or not to recommend its approval by the FDA, Dr. Hussain says it all boils down to one question: Would she want one of her loved ones or her patients to take that drug?

That question guides her, and her fellow committee members, through tricky waters as they ponder the fate of new cancer drugs several times each year. The committee doesn’t examine all new cancer drugs—just the ones where the approval decision isn’t clear-cut and the FDA needs to bring in outside expertise.

The committee’s rulings are important, but so are the discussions they have as they hear evidence about the drug from the company that wants to bring it to market, and representatives of the patients who might take it. The FDA uses both to make its final decision about whether a drug should be allowed on the market.

This past year, her third on the committee and her first as chair, Dr. Hussain found that providing such expertise to a federal agency comes with a heavy dose of public attention. When the FDA ruled that a new immune-therapy drug for prostate cancer shouldn’t be approved because the clinical trial data didn’t show that it clearly extended the lives of patients, a firestorm erupted. Patient advocacy groups decried the finding, and the company that makes the drug was forced to wait until it has more data and can submit the drug for approval once more. But Dr. Hussain and her colleagues stood firm in their opinion that the drug’s benefit needed to be better proven to offset its risks.

Not all FDA advisory committee decisions get so much attention, but they all get made the same way: with hard science driving the hearings and the decision-making process. Dr. Hussain, who is one of several U-M faculty to have served on the panel in recent years, and the first to chair it, says it can be no other way.

Serving on the committee has been an eye-opener, she says, because of the public nature of their hearings and decisions, and because of the tremendous weight that their advice carries at the FDA. Thousands, or even tens of thousands, of people could be harmed if the committee allows an unsafe or inadequately evaluated drug to go forward for approval. But thousands of current patients might see the same drug as “worth the risk,” or hope that even if it doesn’t work for everyone it could work for them. In the end, the panel must balance all of this as it makes its decisions.

Meanwhile, back in Michigan, Dr. Hussain heads another committee that focuses on a different aspect of clinical research: how to make it easier for U-M Medical School faculty to perform clinical research, and be recognized for their achievements.

As chair of the Advisory Council on Clinical Research, she leads a diverse group of faculty from many departments who seek new ways to boost Michigan’s clinical research efforts to the same levels that the basic research community has achieved.

The committee, initiated by former dean Allen Lichter, MD, has been reauthorized by new dean James Woolliscroft, MD, and will continue to play an active role in encouraging and allocating funding for clinical and translational research of all kinds. The committee is endorsing the target of 10 percent growth in clinical research in just five years. By channeling the Medical School’s resources and brainpower toward the pursuit of high-quality clinical research, the committee hopes to bring that goal within reach.
Every woman who gets breast cancer should have the best possible treatment for her individual disease, including the most up-to-date chemotherapy regimens. But even in this age of national cancer treatment guidelines, empowered patients, and comprehensive cancer centers, many women still don’t receive the care that could give them the best shot at survival and a good quality of life.

Why? The reasons are many. But research by Jennifer Griggs, MD, MPH (left), and her colleagues is revealing that factors such as a woman’s race, weight, income, and educational level may have more to do with it than anyone had suspected.

In 2007, Dr. Griggs and her colleagues published two important papers on this topic in the Journal of Clinical Oncology, and began collaborations that will lead to further findings in this area.

In the first paper, published in January, the team found that breast cancer patients who have a lower household income and less education may be more likely to receive reduced doses of chemotherapy, and that severely obese women were four times as likely as lean women to receive reduced doses of chemotherapy.
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Researchers found that doctors were more likely to reduce the chemotherapy dose for heavier patients and those who were less educated, and lived in zip codes with lower median household incomes and higher levels of poverty. Severely obese patients were four times more likely to receive a reduced dose, and women with less than a high school education were three times as likely to have a dose reduction.

When it comes to obese patients, Griggs suggests that doctors might be reducing the chemotherapy dose to avoid giving the large dose that a patient’s weight would indicate—perhaps to avoid potentially severe and harmful side effects. For those patients of lower socioeconomic status, doctors may be anticipating the patient’s attitude toward treatment, especially the side effects that come with aggressive chemotherapy regimens. The “social distance” between highly-educated physicians and less-educated, poorer women may lead physicians to make decisions based on perceptions of a patient’s potential reaction, for instance.

In the second study, published in June, Griggs and her colleagues used another set of detailed patient data from 957 women being treated at 101 oncology practices around the country. They explored whether the women were receiving standard, guideline-based chemotherapy regimens that had been proven to work for the woman’s particular form of cancer.

After controlling for several variables, they found striking differences by race and education level. Specifically, black women were twice as likely as white women to receive non-standard chemotherapy, and women with less than a high school education were more than three times as likely to get non-standard treatment.

Why the discrepancy? Again, many factors are at play, says Griggs, perhaps including the lack of up-to-date information about new treatment guidelines among oncologists in poorer areas, a tendency among

oncologists who treat many types of tumors to “do what they know” for a particular type of breast cancer, and social distancing.

No matter what the cause, these findings from retrospective studies are disturbing enough that a prospective study is needed to see if it can be confirmed among current patients. Dr. Griggs will continue her work in conjunction with Steven Katz, MD, MPH (below), and Sarah Hawley, PhD, MPH, of General Medicine. The research program is also going to focus on the quality of other types of breast cancer treatment, including radiation therapy, through collaboration with Reshma Jagsi, MD, DPhil, in the Department of Radiation Oncology, and quality of pathology information, through collaboration with Daniel Visscher, MD, in the Department of Pathology. With further funding, she hopes to launch a large prospective analysis of medical records from thousands more women, to see if the same patterns emerge.

Though it’s disturbing to see disparities in treatment in a time when they should not exist, Griggs says, it’s only through more research that the reasons behind these differences can be found and addressed.