Transparency in Clinical Trials: Data, Safety and Monitoring of Patients

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Andrew Schorr:
Some people wrote in as we were preparing for this program and they were bitter because they thought they had a spouse, let's say, that had died in a clinical trial. And that relates to a couple of things. One is transparency. Is the data from a trial and any dangers that show up, is that reported and analyzed in public, Jim? And also what are the risks being in a trial, and what is the monitoring to try to have trials be at safe as possible. So, Jim, maybe you could talk about that from a patient perspective.

I want to make sure I know what I'm getting, I know what the risks are, and if any have come up along the way I want it to be reported, and I want to know that there's a team looking out for me.

Dr. Omel:
You have every right to expect that, Andrew. If you're in a trial you have the right to get that knowledge if there's new things that come up that we've learned about. And part of every trial as it's being written, there has to be a data safety monitoring board. These are the experts who will do what you've asked be done. They will monitor the trial as it goes along. They will look for any safety issues. If there are patients who are developing liver toxicities, they will find this. They will point this out and perhaps see if the trial needs to continue or if something needs to be revised.

The presence of institutional review boards review whether trials should go forward or not. Patients who are in trials actually get very, very good medical care and medical coverage. In fact, I would maintain, Andrew, that they get better care than just standard care. They have experts that are watching them even more carefully than would be in a general routine care setting because they're looking for these concerns and problems.

The person who mentioned the bad outcome, we can't ever say that every trial is going to be perfect. There are going to be concerns. That's why trials are done. But they're relatively rare, and we do have boards and review organizations during the trial, not afterwards, but during the trial to be looking out for your benefit, Andrew, so that you're not hurt by the trial.

Andrew Schorr:
All right. But let's say this—and, Mike, for you. So, first of all, admittedly a lot of these trial start, and people are sick people, and they're feeling maybe the trial is their last hope. We had a friend, Lisa Minkove, who died in the CAR-T trial for CLL not long ago. She had been very sick with CLL, so we'd hoped that it would work. It didn't work for her, whether CLL won. And we know other people whereas the learning is going on about often powerful new medicines they didn't benefit. Or in one case, there was a drug, venetoclax (Venclexta) we know about, there were some deaths early on when the drug was far more powerful than was originally understood. So what do we do? I mean that's the real world I guess of scientific study, but that's a concern, you know, Mike, of people saying, oh, my God, I'm worried about being a guinea pig the unknowns on the subject of dangers.

Dr. Thompson:
So there are a couple of things. So whenever people say—it doesn't come up as much recently about being a guinea pig, I say, well, guinea pigs don't have choices, so. And so like Jim has said you can drop off a trial if you want to drop off it. But—so I think for adverse events and things that can happen, one reason to randomize people is that you do understand then if you treat someone with one thing and then another and the death rate the same in both, the drug is not causing it. That's just the disease.

And a couple years ago there was a presentation from the group at Dana-Farber on the precision medicine program, and the issue was they were taking so long to get people evaluated that their performance status or how well they felt was good, and by the time they got through the evaluation many of them had died. Because the disease, you know, when you get to fifth, sixth, seventh-line therapy it can often progress very rapidly.

And so I think that's one of the issues, that people can feel the drug did it, and it's hard to know. And we get these—doctors get these things called adverse events reporting forms, and we have to try to come up with is this probably related, possibly related, and we also get these forms that say you have a patient on the study. The study is open in three countries, thousands of people on it. One person died of a heart attack, and you have no idea as the physician, well, is that the same rate as—you know they're 70 years old. Is that the same rate as this other 70-year-old.

So you need the enumerator and the denominator, and that's what the DSMB or the Data Safety Monitoring Board is supposed to do, which is look at the data and say, is this beyond what we would expect? And they can stop the trial. They can do expanded cohorts. They can do things to try and figure that out.

Now, we know from like even car companies lying about their exhaust systems that if the Data Safety Monitoring Board gets false data, well, you can't fix that. But that's pretty nefarious. Like that I think is not something that's commonly happening and would be a very serious thing to happen.

Now, one thing for transparency is that almost all studies I'm aware of get registered on clinicaltrials.gov or maybe some other sites but usually that site, and they're supposed to report out the outcomes. It's not also a perfect process, but you should be able to see how long the study has been open, are there any complications related to it and those types of things.

So this whole process is not perfect, but I would say in general the people at the companies are trying to develop something they think is going to work. They're trying to do it safely, both to help develop their drug well as well as to avoid a bunch of regulatory issues, and the people on the Data Safety Monitoring Board are trying to do their best to answer these questions. But the smaller the number of patients which increasingly will take the trials we are doing and almost are aiming for, it's harder to be definitive about when these things happen and what caused it.