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Conversation with Anthony Everhart & Tim Meyer:
Increasing the Usefulness of PROs in Oncology Research

Dr. Anthony Everhart, Clinical Vice President for Internal Medicine at Signant Health recently had the pleasure of sitting down with Professor Tim Meyer, Professor of Experimental Cancer Medicine at University College London, and a member of the Signant Health Scientific Advisory Board. They discussed current and future opportunities for increasing the usefulness of patient reported outcome measures in oncology research.

Everhart: Professor Meyer, please tell us a little bit about the research that you're doing in your clinic.

Meyer: I'm a medical oncologist and I work at London's Royal Free Hospital in the Liver Cancer Clinic. My main focus is on drug development. So, I direct the clinical research facility at the Royal Free where we're developing new drugs for the treatment of cancer. There have been many advances in liver cancer over the past few years, so it is an exciting time to be in oncology.

Everhart: Agree, it is a very exciting time. Along with the advances in treatments, there have also been advances in the types of data we collect during oncology research. We have been collecting patient reported outcome measures for some time now, but we've known that, over the past several years, despite a lot of efforts to collect that data, we're not seeing that data used by the regulatory agencies either in some of their decision making or possibly regarding labeling or approval. There may be multiple reasons for that. What do you think some of the issues are with collecting and using patient reported outcome measures in oncology studies?

Meyer: My impression, having incorporated patient reported outcomes in clinical trials for many years, is that generally, the decision by the regulators to approve or not approve a drug is predominantly driven by primary outcomes such as overall survival.

And while the data and how patient reported outcomes are selected are presented, they are not actually used for decision making. And I think one of the issues that I've noticed is that there's a huge amount of variability in terms of the tools used. And there are also issues with the interval in which the data is collected, which is generally made once, once every three weeks or more.

And, when you look at the analysis, there's often a great deal of variability. The confidence intervals are very wide, and that kind of undermines the confidence that this is really reflecting in a granular way what the patients are experiencing. So, I think there is a real need to improve the credibility of these tools to really give us confidence that they reflect the patient experience.

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Everhart: One of the things you mentioned was regarding the increased spread in the confidence intervals. Do you think that is related to the specificity of the instruments themselves, that they may be asking questions too broadly with a lot of overlap? What do you think may be causing those wide confidence intervals?

Meyer: I think that must be part of it. One of the observations that's very striking is that if you look at a randomized controlled trial comparing to a drug you know to be toxic with placebo, and you look at the longitudinal assessment of quality of life, you often see no significant difference and the confidence intervals overlap.

But your experience is that the patients are having significant side effects, which are influencing their quality of life. Therefore, you know that these instruments are not really reflecting what's going on.

Everhart: Is there also a problem with the overlap between the disease course itself and the treatment and in differentiating the quality of life effects from those two contributing factors?

Meyer: Absolutely. We commonly see that the patient's quality of life will improve or the deterioration in quality of life will be less if you are using an effective drug, and that clearly has an impact in addition to the toxicity that they experience. The other thing that influences the course of quality-of-life changes is what's actually happening with the dose of the drug.

When a patient starts treatment, if they experience side effects, it affects their quality of life, and the physician may have to reduce the dose. That means that quality of life may improve, and unless you know what's going on at a very granular level with each patient in terms of the dosage, what's happened with disease, it's difficult to interpret what's happening with changes in quality of life.

Everhart: One of the other things you mentioned was the frequency at which we collect this information. Traditionally, in most oncology studies, these patient reported outcome measures have been collected around the start of the new treatment cycles. Recent regulatory guidance, particularly from the FDA draft guidance, suggests that we should increase the frequency of sampling because we're missing a lot of inter-visit data. Do you think there's room to increase the frequency of collection of patient reported outcome measures in the oncology studies, even if that means moving to remote collection where patients would be providing more of that information through completion of assessments at home?

Meyer: Definitely. Having more frequent assessments would be vital, particularly when drugs are given in a discontinuous schedule and patients have fully recovered from their side effects by the time of the next cycle, and I think completion of patient reported outcome measures at home is certainly the way to do that so that patients don't have to come in for extra visits at the hospital for that. I think that, with the way technology is moving, the future is going to be with that kind of remote collection of data including actigraphy. This will give us that much more granular data, and that may well complement more complex questionnaires that we are administering currently.

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Everhart: So, you mentioned actigraphy. Do you believe there's a place in oncology research to increase the use of sensors and wearables to collect more objective data, be it passively or actively, to supplement some of the data that we collect alongside patient reported outcomes? Would that help you as a practicing clinician to better manage patients, would be informative to the regulatory authorities when it comes to the assessment of efficacy, or a combination of the two?

Meyer: A combination of the two. Firstly, as a clinician managing a patient, it is often quite difficult to really assess the impact of treatment on patients' lives. Many patients will report lethargy or tiredness. But, having a constructive read-out of that in terms of activity would be very useful in making decisions about dose reduction, for example. I think similarly for the regulators, having greater confidence and a more constructive objective assessment of the impacts of treatment will become increasingly important, particularly as more trials become driven by softer endpoints in addition to primary endpoints such as progression free survival.

Everhart: Thank you so much for your time, Professor Meyer. This was very informative.

Tim Meyer, MD PhD, is Professor of Experimental Cancer Medicine at UCL Cancer Institute and Honorary Consultant in Medical Oncology at the Royal Free Hospital. He is the Director of the Royal Free London Clinical Research Facility and Clinical Lead for the hepatocellular carcinoma service at the Royal Free Hospital where he leads a large portfolio of clinical trials. He is the Cancer Director of the NIHR Wellcome UCH Clinical Research Facility and the Joint Director of the UCL ECMC. Nationally, he chairs the TRANSNET Committee, is a member of the UKNETS Steering Committee, and sits on both the Hepatobiliary and NET NIHR Clinical Studies Sub-Groups.

Dr. Everhart is the internal medicine leader at Signant, where he oversees the clinical application of Signant's digital health technologies and services for general medical indications. He received his medical degree from the Quillen College of Medicine completed his residency in the United States Air Force. Dr. Everhart is board-certified in internal medicine and a fellow of the American College of Physicians with over 25 years of experience in the practice of medicine and over 15 years of experience in clinical development. He regularly contributes to thought leadership through publications, webinars, and panel discussions. He currently serves as Signant's representative on the Decentralized Trials & Research Alliance (DTRA) Leadership Council. He has worked in all phases of clinical development and is currently the Scientific Lead for Oncology, Hematology, Dermatology, Rheumatology, Respiratory studies at Signant.

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