'Everyone is an individual': providing individualized treatment in oncology

Michael A Thompson* speaks to Stella Bennett, Commissioning Editor:

Michael A Thompson, MD, PhD is a hematologist/oncologist and researcher at Aurora Health Care (AHC) and the Aurora Research Institute (ARI). Dr Thompson is a native of Minnesota. He received his BS degree in Molecular Biology from the University of Wisconsin – Madison, his MD from Mayo Medical School and PhD in Molecular Pharmacology and Experimental Therapeutics from the Mayo Graduate School. He completed his Internal Medicine Residency at the Mayo Clinic College of Medicine. He obtained his

Hematology/Oncology Fellowship at the University of Texas MD Anderson Cancer Center. Dr Thompson received the American Society of Clinical Oncology (ASCO) Young Investigator Award in 2006 and the American Society of Hematology Clinical Research Training Institute (ASH CRTI). After fellowship, he moved back to the Midwest, where he served as the Medical Director of Cancer Research at ProHealth Care Regional Cancer Center, as well as the local site Clinical Trials Lead Investigator of the NCI Community Cancer Centers Program (NCCCP) and national Co-Chair of the NCCCP Clinical Trials Portfolio/Accrual Log Working Group. He also was on the NCCCP Early Phase Working Group which focused on bringing new drugs to the community setting. In 2013 he joined AHC as the Medical Director of the Early Phase Cancer Research Program. Dr Thompson was a recipient of a Vince Lombardi Cancer Foundation (VLCF) funded Aurora Cancer Care Research Award (ACCRA) 'The Immune Response Following Vaccination in Multiple Myeloma Patients' which is an ongoing Aurora-based research study. In 2014, AHC received the NCI Community Oncology Research Program (NCORP) grant. Dr Thompson is the co-primary investigator. Dr Thompson has studied and published in the area of hematologic malignancies – myeloma, lymphoma, leukemia and other cancers. He is on the ECOG Myeloma Core Committee and the NCI Myeloma Steering Committee. He has a strong interest in clinical research in hematologic cancers as well as in new drug development in a variety of cancer types. He is currently on the ASCO Cancer Research Committee, ASCO Community Research Forum, and on various research subcommittees. He is active in social media (Twitter: @mtmdphd) with national presentations on the topic of the use of social media in oncology.

Q What would you say influenced you to pursue a career in medicine?

I was always interested in science, but I thought that the most interesting things to research were complex organisms like humans. I did an MD PhD because it

balances bench research, which is very basic and can lead to huge discoveries but often takes a lifetime of work, with clinical medicine which allows you to help people immediately, sometimes. Whenever I am just seeing patients I am very interested in

KEYWORDS

- ASCO • precision medicine
- social media • Twitter

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research, and when I am doing research I am very interested in getting back to the clinic so I think there is a tension and balance that helps me do what I do well.

Q What led you to specialize in medical oncology & hematology?

I started off in medical school interested in neurosurgery, and neurosciences, and I did my PhD in pharmacology. They were studying pharmacogenetics, which is now called pharmacogenomics, and in my more in-depth study of pharmacology it seemed that the most important issues in pharmacology were those with drugs involving a narrow therapeutic index. Such as some drugs used in chemotherapy where there are benefits, but the risks are high, too. Therefore, I specialized in this field because of my interest in pharmacology as well as the knowledge that a lot of research dollars were heading in the direction of cancer research. Cancer is an important human health issue. Cancer is complex and can take a lifetime of work, and I thought that was an interesting area to go into.

Q Your interests include clinical trials, translational & basic science research. Can you tell our readers briefly about any research projects you are currently working on?

A lot! In my new job, I was brought in to increase our industry studies, so we have been increasing our cooperation with pharmaceutical companies, bringing health trials to Aurora healthcare [1] which is a large healthcare system in Wisconsin. I started about 2 years ago, and soon after I joined we applied for and subsequently received National Cancer Institute (NCI) funding for the NCI Community Oncology Research Program (NCORP [2]). As a new NCORP site we are increasing our accrual to NCI trials. I have collaborated on the submission of an NIH R21 grant on medication adherence using an iPad app. We are studying multiple myeloma, where one of the major reasons people die is infections and vaccination response. We also do not have a lot of information on how many people are getting vaccinated at all, or using other infectious prophylaxis. We are doing a study that is funded by the Vince Lombardi Cancer Foundation [3] looking at myeloma patients and control participants (who do not have myeloma) on what their antibody and other immunologic responses are to standard vaccinations with influenza and pneumococcal pneumonia. There

is some information in the literature going back to the 1980s but very few studies. I think these data will inform us on a major supportive care approach we can take for multiple myeloma patients as well as potentially looking at mechanisms with newer myeloma drugs such as thalidomide, lenalidomide and pomalidomide as well as bortezomib and carfilzomib that may have an influence on how we think about immunoncology therapies in multiple myeloma and other hematologic cancers.

Q You have said “everyone is an individual. My goal is to offer patients personalized precision medicine for their unique situation.” How have you seen the field of precision medicine in cancer develop during your career?

Precision medicine is a buzzword. It has some utility, and I use it just because people kind of know what I am talking about, but I think ever since there were physicians treating patients there has been the idea of personalized therapy. Personalized may have meant dealing with someone's social situation, their economic situation, their family or values, all sorts of things. When we did not have many drugs there was not much to personalize from a therapeutic standpoint. If someone had pneumonia and you had one antibiotic, that is what you used. If someone had a blood clot and you had unfractionated heparin, that is what you used. Now that we have gotten more therapies and our health system has gotten more complex, there is more to personalize. So when people talk about precision medicine they are generally talking about molecularly guided personalized medicine. There is hope that by doing this it will lead to better therapies and even more, value and cost-effectiveness. We know that not all precision medicine is curing people, or even helping everyone, and so I think we need to look at precision medicine as hypotheses to test rather than as facts. Part of the hype of precision medicine is people are confusing theory with hypotheses to experimentally test. That is why we need to do clinical trials to see if some of these concepts we think will work actually do work in real-life situations.

Q Do you feel that medical practitioners need more education regarding offering individualized treatment for patients, rather than trying to adopt a ‘one-size-fits-all’ strategy?

Yes. Just recently, from the ASCO 2015 meeting [4] this is a huge topic and something everyone is struggling with. We are getting an explosion of therapy options, and even the most academically oriented, limited disease type physicians are struggling to keep up. People have looked at a variety of mechanisms to try integrate clinical and molecular data including services such as IBM Watson and Oracle systems or Syapse to integrate complex data into electronic medical records. There are companies like Paradigm, Caris and Foundation Medicine [5] that are dealing with this complex interplay of host changes in the human and tumor changes. It used to be a world where you could say "this person has lung cancer with an *EGFR* mutation" and treat that, but we are increasingly understanding that there are more mutations than one. Cancers are often heterogeneous within the same patient and tumor, and cancers change over time. We have issues of what mutation and where are those mutations geographically in the body. Understanding mutation load over the dimensions of time and space can allow an appreciation of the beyond single driver mutation. There are networks of signaling pathways that are affected in cancer and host tissue. It is getting very complicated, but when medicine gets complicated that is generally good for the patient. It means we are understanding things and moving forward. Part of understanding is appreciating how much you do not know. While we have made great strides in medicine there is still much we do not know and in some cases we have to go back to the bench to do some research. We just have to move more quickly to go between the patient and bench in a real-time manner, and that is starting to happen.

Q You were on the NCI Community Cancer Centers Program Early Phase working group which focused on bringing new drugs to the community setting. What were the main outcomes of this working group?

That was a group that looked at early phase clinical trials through the NCI Community Cancer Centers Program (NCCCP; which was one of the community research programs that existed before the NCORP) [6]. We shared best practices and talked about issues with early phase cancer clinical trial. 'Early phase' studies can mean Phase I or II. Many trials that are opening currently are Phase II, so given that 85% of patients with cancer are in the community and

historically around 50% of accruals have been in the community setting many community sites are currently performing early phase cancer research. Early Phase I studies are more resource intensive, but we learned that some community centers are certainly capable of accruing to Phase I cancer clinical trials. We sometimes see this come up with a company that wants only to deal with academic centers and we know that many Phase I trials do not need to go to larger academic centers and that they may benefit patients from having access to a larger population and more real-world populations such as in the community.

Q What is your role on the ASCO Cancer Research Committee?

ASCO is a large professional organization for oncologists, and it is called the American Society for Clinical Oncology but really it is international in scope and participation. About half of the people who attend the ASCO meeting come from outside the USA. ASCO has many committees, covering lots of different areas, one of which is the ASCO Cancer Research Committee. One project from this committee was to update the ASCO policy from 1997 on the critical role of Phase I trials in cancer research and treatment. I was part of that writing committee, and we produced the policy update in mid-December 2014. I think that was a useful update, and one of the things that I added to that document was that therapeutic intent was always present in Phase I trials. When I have tweeted that information out people have either argued "oh no, it's not," or have realized "I guess it is," and this is from the NCI investigator handbook. That is important because some insurance companies have tried to deny coverage of Phase I trials because they say there is no therapeutic intent. There is this statistical power to look at safety, but there is always therapeutic intent, so I think that one of the big things that I was involved with was propagating that information.

Another project from the ASCO Cancer Research Committee (CRC) with Drs Schilsky and Kim involved the Targeted Agent and Profiling Utilization Registry (TAPUR) study. The concept was described by Dr Schilsky in *Nature* in 2014 [7] and has been discussed at:

- TAPUR Study – via @ASCO [8] #ClinicalTrials;

- TAPUR Study Frequently Asked Questions (FAQs) – via @ASCO [9].

The ASCO CRC also helps organize the educational agenda for the ASCO Annual Meetings and other meetings. One spin-off of the ASCO CRC was the creation of the ASCO Community Research Forum [10]. The ASCO CRF is an environment where people working in a community study could get it together and discuss issues relating to main points in a community setting. I have been working with past chair Nick Robert, MD and chair Skip Burris, MD. We have an annual meeting in the fall which is attended by people from all over the country, and often from industry, NCI, US FDA, where we talk about issues in the community. That has been one of my major focuses in the last year or two, and I will be ramping up this focus as I become chair of that in 2016. Issues we are reviewing include credentialing and understanding what community resources are available both nationally and for each individual site, looking at contracting and barriers to accrual as well as research workload issues.

Q You are very active on social media platforms such as Twitter. How important do you think social media use is in oncology?

I think it is important, but what we know is that despite increases in the number of oncologists on social media including Twitter that it is still a minority of oncologists that are participating. Not every oncologist needs to utilize social media, but I think – and we really saw this at ASCO 2015, where they recommended that people follow a variety of tumor types – it does help draw out conversation, and highlight important points from meetings. In the past, these conversations might happen months later, in the oncology newspapers that we all receive, but now this is happening in real time. Oncologists who are not at the meeting – maybe rounding in the hospital – have told me they felt like they had been there and they really appreciated getting that up-to-date. Also, PhD researchers not attending the meeting may gain clinical insight into what the MDs are talking about.

Other interested groups include patient advocacy groups, stock analysts and the general public.

There are myths about cancer and clinical trials. A more informed population with an improved knowledge base is important to support research. We need to support educating everyone about what cancer research is doing and why it should be funded, why it is important, and also increasingly have discussions about why it is of value.

Also, we need to say, even if we can do something that is very expensive, should we do it? And really start having more transparent conversations about the costs and value. We need to figure out the best way to use therapies or to decrease costs to benefit individuals and society.

Q Finally, do you have any closing thoughts for our readers?

I would say we are in a very exciting era of oncology, where we have already made great strides in improving the outcomes for many cancers. For some cancers we have not changed survival much and I think we need to raise awareness about the role of basic science research and really cherish patient participation in clinical trials. Because that is the only way we move medicine forward, by systematic critical evaluations of potential therapies and between precision medicine and immuno-oncology we are going to start curing more cancers in the next few years. I also think we are going to improve outcomes for cancers we cannot cure now.

Disclaimer

The opinions expressed in this interview are those of the interviewee and do not necessarily reflect the views of Future Medicine Ltd.

Financial & competing interests disclosure

MA Thompson has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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