Interview with Dr. Eitan Amir

UTMJ Interview Team (Nayantara Ghosh and Kevin Si)

Dr. Eitan Amir

Eitan Amir, MB, ChB, PhD, is a medical oncologist at the Princess Margaret Cancer Centre in Toronto and an Associate Professor in the Department of Medicine at the University of Toronto. Dr. Amir also serves as the Cancer Care Ontario Systemic Therapy Lead for Toronto Central South, as well as the Vice-Chair of the Cancer Research Ethics Board at University Health Network. He received his medical degree from the University of Manchester, United Kingdom. He stayed at the University of Manchester to complete his residency in internal medicine, followed by his specialty training in medical oncology. Subsequently, Dr. Amir completed a PhD in Clinical Epidemiology at the University of Toronto.

Dr. Amir has over 150 peer-reviewed publications, in addition to numerous published abstracts and book chapters. He has been honored by the American Society of Clinical Oncology & the American Association for Cancer Research with numerous research awards. His clinical interests include investigating different aspects of breast cancer treatment as well as the toxicities of anti-cancer drugs. His academic interests include clinical trial methodology, meta-analyses, and outcomes research.

UTMJ: Can you tell us a little bit about yourself?

EA: I am Eitan Amir, and I'm a medical oncologist here at the Princess Margaret Cancer Centre. I also do a single clinic at Mount Sinai. I'm also an associate professor in the Department of Medicine at the University of Toronto. The way that things work for academic clinicians in the Department of Medicine is that there are a number of different tracks that you can be appointed to. I'm a clinician investigator, which is somebody who is expected to spend about 50% of their time on clinical work, and then 50% doing other things such as research, teaching, and administration. As for me, I treat breast cancer only since medical oncologists are now highly specialized! You don't really have a general oncologist anymore, especially not in academic centers. Most of us do a single disease site, or maybe two disease sites. By disease site, I mean, for example, GI – which includes stomach, pancreas, liver, colon, rectum, and anal cancers. Oncology is typically an outpatient specialty, so I spend probably over 90% of my time seeing patients in the outpatient clinic, and very little time doing inpatient work. There's a lot of us at Princess Margaret Cancer Centre – we have over 50 staff across medical oncology and malignant haematology, so working out-of-hours is really quite limited! I do two weeks of attending per year, and maybe two to three weekends! In terms of my research, it is split mostly into health services based research. I do a lot of evidence synthesis, which is basically going out into the literature and re-analyzing available data. We do a little bit of large database work, especially through the Institute of Clinical and Evaluative Sciences at Sunnybrook Hospital. I also direct the fellowship program here at Princess Margaret. A fellow is someone who has completed their residency program in internal medicine and the medical oncology program and is doing some additional training. Finally, I'm also the vice-chair of the cancer ethics board here at UHN. That obviously involves a lot of administrative work about running a trial, making sure that the process is done in a way that's safe to patients. So that's me in a nutshell.

UTMJ: We were quite interested in your role as the Vice-Chair of the Research Ethics Board at UHN. What advice do you have for someone who's starting a research project in cancer? For example, what are some ethical concerns someone would run into?

EA: Well, I think it's really quite straightforward. In Canada, we have something called the Tri-Council Policy Statement. It's very easy – it's training anybody can access and complete, including medical students. It's free, and you can complete it online. GCP (Good Clinical Practice) is something that you can get involved in as well, usually as a resident, although I don't know how easy it is to access because it's usually done in individual institutions. Between these two training programs, a lot of the core ethical principles of research are very clear. The Tri-Council Policy Statement training is probably two hours to complete, so it doesn't take very long. As for my role

on that committee – typically, in these committees, we have a chair and the chair is somebody who is basically a retired clinician who still wants to participate. It takes quite a bit of time to be in this role, and you can't really be the chair of an ethics board and still have a clinical practice. I cover for the chair if he's away. Since I competed a PhD in clinical epidemiology here at U of T, after my residency training, a lot of what I was trained in was research ethics. So, quite often, I see my role as trying to solve problems regarding research methods. Most of the trials we see at the ethics board are multi-centred trials that are run not only in Canada, but frankly, in multiple centres all over the world. They're written by industry, they're usually very good…and so your ability to change anything is usually quite limited. But there are a lot of investigator-led projects that get reviewed as well, and obviously that is where we have a lot more leverage. Unfortunately, the quality of some of these applications is a little less strong. Quite often, a lot of the input we provide is about how you've written things, if it makes sense and whether it really meet the criteria for Tri-Council, GCP, or any of the other standards that are present and accepted by pretty much all academic institutions around the world. As a member of the research ethics board, you have to review studies or applications that come through. We have one meeting every month, and we are by far the busiest board at UHN! This is mostly because cancer is such a research-oriented field. It can take two to three hours to complete a full application. You have to read the protocol, the informed consent documents, and it is important that they are clear and that there aren't any major questions that may need to be resolved from a patient safety perspective. Typically, we'll do one or two of those a month, plus a half day that the meeting itself takes. So, the ethics board takes about a day of my month.

UTMJ: You mentioned that a lot of your research focuses on health systems work, and looking into what the evidence already says. We would imagine that with cancer therapy being such a hot topic, there is always new evidence being generated about cancer therapy. In your time as a researcher, have you seen any trends in the way that cancer therapy research is being conducted? Or the things that people are focusing on now?

EA: There's no doubt that there are some very clear trends that have emerged in the past while. One is that research is increasingly being funded by industry and less funded by non-profit agencies, such as governments or charities. That's very clear to us. Trials in general are getting bigger, not using definitive end points as often, and are increasingly using intermediate end points that are more suspect. So, now, there's a bit more of a "spin" in terms of how things in the literature are being reported. On the other hand, we are also increasingly seeing the use of complex math to try and find new solutions to old problems. Quite often, you can try and pull data from different locations to find some kind of pattern that may be helpful in the treatment of patients. I think I've been quite lucky, certainly as part of my PhD, but also thereafter. By looking at some very simple studies, some of which just relied on collecting information on secondary outcomes from different trials and pooling them together, I think we've managed to change the way people think about certain things in oncology! Our research has influenced major guidelines, and people's thoughts on how to choose treatments can be based upon that. I think that it's nice to see that. So, there's good bits and bad bits to the emerging trends in cancer therapy research.

UTMJ: Are there any specific guidelines or things of that nature that you've seen change?

EA: The majority of practice change in medical oncology relates to new drugs… it's very rare that old drugs get any interest. I'll give you an example of how evidence synthesis helps in breast cancer: We now know that giving bone therapies, like bisphosphates (that are used in osteoporosis) in different doses can reduce the risk of breast cancer death in women who are postmenopausal. All the trials individually were not positive, because we didn't really understand that this was going to be a treatment that would only help menopausal women. It wasn't until people decided to pool all of the trials together and separate them up into premenopausal and postmenopausal that we had enough power to identify this relationship! In addition, I think that we've learned more about the side effect profiles of certain drugs. Although some side effects are uncommon, they can be very serious. Individual trials just don't have enough power to identify these, since the purpose of these trials is to look at efficacy! You will miss certain side effects. To prevent this, we need to pool things together and gain enough power to explore different side effect profiles. We've done a lot of work on side effect profiles in terms of systematic reviews and meta-analyses. I think we've identified certain side effects which are important in the general management of patients. Ultimately, what is most satisfying is that this work has led to the for-

mation of clinical programs. For instance, we've instituted large cardio-oncology programs on the basis of a lot of work looking at the effects of both cancer and cancer treatment on heart disease. I wouldn't say all of this is my work – but I think we've certainly contributed substantially to cardio-oncology both locally and internationally.

UTMJ: Along those lines, where do you see drug treatment in cancer and cancer research going in the future?

EA: I think we'll keep on seeing what we're seeing right now. I think we might get a little bit more sophisticated in trying to find subgroups of patients. For example, the most common type of cancer that is diagnosed is lung cancer, and the most common type of that is non-small cell lung cancer. However, now, you can split non-small cell lung cancer into multiple little groups depending on the type of non-small cell lung cancer. Some of these groups are extremely small, but they have completely different treatments. So, as you get a bit more sophisticated in identifying these subgroups, you're splitting disease – defined by where the cancer started – into smaller groups. These are groups that have less than 100,000 people within it diagnosed in the United States, or maybe 10,000 in Canada, in a year. These are actually quite uncommon diagnoses! However, it's important to note that their treatments vary widely, and it's important to know what they are for each individual patient. Also, there's obviously going to be a lot more interaction with technology, which may be due to the huge improvement in accessing genomic technology or in terms of circulating genomics. I don't think we've made as much progress in this realm as we should have by now, but it is a bit tricky. I think artificial intelligence will be very interesting because it will hopefully help us to analyze these enormous datasets in a way that we are currently unable to do. They're just slightly more sophisticated ways to look at data than standard statistics, which is what we've been doing for the last hundred years.