Interview with Dr. Philippe Bedard

UTMJ Interview Team (Annie Yu and Ryan Daniel)

Dr. Philippe Bedard

Biography

Dr. Philippe Bedard has a clinical practice and a research program. His clinical practice includes the treatment of patients with breast and testicular cancers. His research program involves early phase clinical trials with novel cancer drug treatments. These emerging treatments include immunotherapy and the personalization of cancer treatment based upon the results of testing for DNA mutations within tumor cells.

Interview

UTMJ: Hi Dr. Bedard, would you mind telling us about your clinical and research work?

PB: My name is Philippe Bedard and I am a medical oncologist at the Princess Margaret Cancer Centre and the Clinical Director for the Cancer Genomics Program. As a clinician-investigator, my clinical practice is focused on breast and germ cell cancers and my research is in the area of experimental phase therapeutics, early phase clinical trials, and clinical genomics.

UTMJ: In your mind, what is the definition of personalized medicine?

PB: Personalized medicine, or precision medicine, is guided by information about individual variability that can be applied to clinical decision making. For cancer treatment, personalized medicine can include using germline or somatic genetic variation to inform the selection of drug treatment based upon an increased likelihood or response or avoiding a drug treatment because of an increased risk of side effects.

UTMJ: Could you elaborate on the current landscape of personalized medicine and its use in the field of oncology?

PB: Oncology is rapidly evolving. Oncologists are often organ-site specific – as a breast tumour oncologist, I treat tumours that start in the breast. Drug treatments for breast cancer are very different than drug treatments for lung cancer or brain tumors. Even a few years ago, we had very limited penetration of tumor sequencing and limited understanding about how differences in tumor or germline genetics might influence prognosis and response to drug treatment. There are now many examples of drug treatments that are effective only for subpopulations of patients whose tumors harbour specific oncogenic driver mutations. But our clinical practice has not kept pace with advances in sequencing technology and large-scale sequencing projects that have characterized the genomic landscape of most cancers. Today, clinical genetic testing is mostly single gene testing or testing of a small panel of genes that characterize mutation hotspots. We're just scratching the surface of applying genomic testing to cancer medicine.

UTMJ: How do you predict the field to change in the next 5-10 years?

PB: Technological advances and the development of new drug therapies that require more comprehensive genomic testing will drive practice changes. We'll have greater access to genomic tests at a lower cost. All patients diagnosed with cancer will have tumor and germline genomic testing in addition to standard histopathological diagnosis and TNM (tumor, nodal status, and metastasis) staging. Through analysis of genomic signatures, we'll better understand the mutational processes that led to the development of a patient's cancer. We will have more comprehensive databases of genomic testing results linked to clinical phenotypes, to have a better idea about how other patients who have a similar type of genomic profile fare on standard treatment. We'll have the ability to dynamically monitor genomic alterations in a patient's primary tumor using blood tests (known as circulating tumor DNA). And hopefully at some point we'll be able to actually intercept treatment-resistant subclones detected in the circulation and prevent the patient from developing metastatic disease. It takes time to reach this utopian future of genomically-guided cancer care. One of the biggest bottlenecks that we as a research community are struggling with is collecting detailed clinical data, such as the treatments that patients receive in the metastatic setting and their response to treatment, to link to genomic testing results. The challenge is that this type of information is not easy to

obtain from our medical records; patients move around, many paper based results are scanned into our electronic medical records, and even in a single payer publicly funded health care system, we don't have a universal, harmonized medical record system.

UTMJ: Do you see advocacy towards changing access to clinical data or is this just something that you accept and you have to adapt your research work for?

PB: Most patients in my practice are very motivated to participate in research. We've run a number of genomic characterization studies that involve multi-gene testing of stored tumor tissue and/or blood samples and anonymized data sharing of clinical data with other cancer researchers. We explain to patients that the likelihood that this type of research genomic testing will lead to a change in treatment for their cancer is low. In spite of this, the vast majority of patients approached agree to participate. I think the barriers are time – everyone's hard pressed in the medical system – and resources are limited. Healthcare is extremely expensive and complex. We struggle to pay for expensive new cancer drugs and our health care infrastructure is not designed for iterative learning that can be applied to future generations of cancer patients. But we're going to be forced to change. Patients have access to test reports in real time, sometimes before their healthcare providers – I think this makes them better informed about their treatment. Sometimes it causes additional anxiety, but they have more awareness of what's going on in the healthcare system rather than accepting what the doctor tells them as absolute truth. With better access to their records, patients are more actively seeking opportunities to participate in research and, in some cases, are sharing their health care records through large scale research projects to try to accelerate discoveries that can be applied to patient care.

UTMJ: Building on that, can you tell us more about the AACR-GENIE (American Association for Cancer Research Genomics Evidence Neoplasia Information Exchange) Project that you're working on, which is directly linked to the accumulation of reliable clinical data?

PB: GENIE recently celebrated its 5th anniversary. It is a collaboration of academic cancer centres with institutional sequencing initiatives to pool and share their data with the wider research community. The fundamental principle behind GENIE is we can learn more through data sharing as a collaborative than any single centre could through sequencing its own patients and keeping their data in house. The project initially involved 8 centres and now it involves 19 where we share genomic and clinical data. The current release has more than 70,000 clinical and genomic records from patients mostly with advanced cancers. Traditionally, there are barriers to sharing clinical and genomic data between hospitals, so it is impressive that GENIE has aggregated such a large number of records in a short period of time that can be accessed by any researcher. The biggest challenge with GENIE is that clinical annotation is limited – with more than 70,000 genomic records it would be great to know how each individual patient fared with their cancer treatments, how long were they on treatment, whether or not the treatment worked, what were the side effects, and what were the reasons the treatment stopped, so that we apply these data to avoid ineffective therapies in other patients and identify genomic subpopulations that might be particularly sensitive to specific drug treatments. There is great hope that digital tools like natural language processing and automation will create accurate clinical records, but at the present time, a trained data coordinator is still required to read through a patient's records and extract information that can be entered into a database in a standardized manner to harmonize data collection across sites.

UTMJ: Could you clarify the challenges of trying to link the clinical data to the genomic data?

PB: The clinical data that we have in GENIE is limited to simple parameters like age, ethnicity, interval between cancer diagnosis and relapse, type of cancer, etc. Even for a seemingly straightforward variable like "type of cancer", it is actually quite hard to get 19 hospitals use the same ontology. These challenges are not unique to GENIE as a project. Any type of large scale clinical project struggles with this type of issue due to the complexity of modern medicine. More comprehensive clinical data can be accessed; the challenge is having adequate resources at the sites to extract that type of information in a way that can be shared and that can accelerate new discoveries.

UTMJ: Switching gears to another domain you work in, what are some challenges with being involved with early phase clinical trials, considering you're really at the cutting edge?

PB: Early phase clinical trials typically enrol cancer patients with advanced refractory disease, or patients with a type of cancer where there are either no effective treatments, or patients whose disease has progressed after standard therapy. These trials are increasingly complex, in terms of cost, administrative oversight, and identification of trial participants. From a patient's point of view, it is a very big commitment to take part in an early phase trial. Patients have to visit the hospital frequently, especially during the first few months of a trial, for monitoring and study related procedures, like additional blood sampling and tumor

biopsies to better understand if a new drug is actually hitting its target.

UTMJ: I know you just touched on the patient perspective, but what was your personal perspective in terms of integrating the patients from your clinical practice into clinical trials?

PB: It's exciting to be able to offer these trials to patients. Patients enrolled in an early phase clinical trial receive a very high level of care, including a direct contact with a clinical trials nurse, and close monitoring by the study team, I enjoy being part of a research team that includes staff physicians, clinical research fellows, nurses, pharmacists, data coordinators, and correlative studies technicians. We work closely together to make sure that patients are very well looked after and that we collect high quality data to maximize what can be learned from patient participation. As a medical oncologist, early phase trials are also exciting because these are treatments that are completely new and require the use of a full range of clinical skills to try to sort out whether adverse events are related to patient's disease or are a side effect of a new drug. It is also demanding to look after patients with advanced cancer and limited life expectancies. Patients often view early phase clinical trials as their last hope, and it is difficult when a new drug treatment does not live up to their expectations.

UTMJ: What advice do you have for medical students and trainees as they begin and progress in their careers?

PB: As a trainee, your focus is always doing well on the next exam, or trying to put yourself in the best position to get into a residency or fellowship program and eventually a full-time staff position. Keep in mind that you've invested a lot in your training and your career arc extends well beyond your training. It's hard to see that when you're in the weeds of trying get through medical school or postgraduate training. The best advice I have is to follow your passion: find out what really gets you excited and what you really enjoy doing on a day-to-day basis. Becoming a physician is a great job, but it has its challenges. It's important to find what motivates you and make sure that you follow it.