Patient Case: JR is a 52-year-old mother of four who was diagnosed with chronic myelogenous leukemia (CML) in 2002. Over the last 13 years, she has been treated with a number of tyrosine kinase inhibitors (TKI), which have kept her cancer at bay. However, since she was switched to a new TKI, called nilotinib (Tasigna), she has developed diabetes and now presents with claudication in her left leg. She is referred to the Cardio-oncology clinic for management of her cardiovascular issues. The referring oncologist also wants to know whether her most recent treatment is responsible for her cardiovascular problems.

Cardio-oncology (the cardiovascular care of cancer patients) has emerged as a new discipline in medicine in part due to the explosion of novel oncologic therapies, which have dramatically changed the natural course of cancers and have introduced survivorship as a new theme in oncology care. Many of these therapies can have side effects on the heart and vasculature. In addition, since cardiovascular disease is prevalent in the general population, cardiac disease represents a major burden for cancer survivors (15 million Americans in 2015).

Cardio-oncology is not a new field. Forty years ago, cardiovascular issues were observed in patients, particularly children, treated with anthracyclines and radiation. However, these treatments were nonspecific and cytotoxic. The advent of more selective, mechanism-based therapies more than a decade ago led to hopes for an improved safety profile. An early example was trastuzumab (Herceptin), the first drug targeting the erbB2/Her2 signaling pathway, which is overexpressed in a subset of breast cancers. However, despite trastuzumab’s oncologic success, a significant percentage of treated patients developed heart failure. Bevacizumab (Avastin), which targets a signaling pathway important for angiogenesis, has been highly successful in the treatment of some cancer types but is associated with hypertension, thrombosis, and cardiomyopathy.

The Vanderbilt Cardio-oncology Program

The Vanderbilt Cardio-oncology Program brings together clinicians and researchers who collaborate to understand the complications associated with traditional and new cancer therapies. This multidisciplinary program has several current cardio-oncology research at Vanderbilt:

- Effects of TKI on the cardiovascular system
- Mechanisms of toxicities for newer cancer drugs
- Genetic changes that modify the cardiovascular effects of cancer therapies
- Risk factors that predispose individuals to both cancer and cardiovascular disease
components, including cardiovascular care of cancer patients, basic and translational research, and training of the next generation of cardio-oncologists.

In the past, heart failure was thought to be the main complication associated with cancer therapies, but recent drugs have been associated with vascular complications (including hypertension), metabolic derangements, thrombosis, and arrhythmia. As a result, our clinical program consists of clinicians with varied expertise. Daniel Lenihan, M.D., and JoAnn Lindenfeld, M.D., are interested in cardiomyopathies that arise in cancer patients. Dr. Lenihan also directs the Vanderbilt Amyloidosis Multidisciplinary Program (VAMP), a comprehensive clinical program providing care for patients who have suspected or confirmed amyloidosis. David Slosky, M.D., and Javid Moslehi, M.D., are investigating vascular and metabolic complications that arise in cancer patients.

In addition, the Vanderbilt Cardio-oncology thrombosis center has a special interest in thrombotic disorders in oncology patients. Finally, recognizing the importance of cardiovascular health in cancer survivors, our group has developed a cancer survivorship program. One component of the program is an innovative approach known as the “ABCDEs,” described by Moslehi and colleagues.4

A distinguishing feature of the Vanderbilt Cardio-oncology Program is close interaction between clinicians, physician-scientists, and researchers. Thomas Force, M.D., is a physician-scientist and past president of the Heart Failure Society of America who is an international authority on cell signaling in the heart. Dr. Force has defined the roles of kinases in the cardiovascular system and how specific TKI, used for cancer therapy, perturb this system. Dr. Moslehi is interested in the mechanism of toxicities for newer
drugs, including ones that target the protein degradation machinery of the cell. In addition, Drs. Moslehi and Lenihan have a number of ongoing clinical studies designed to translate these basic research findings into clinical practice. Cardio-oncology investigators are also leveraging Vanderbilt’s BioVU, the largest biorepository at a single academic medical center worldwide, to explore genetic changes that modify the cardiovascular effects of cancer therapies. Research efforts are also directed toward understanding mechanisms by which common risk factors can predispose patients to both cancer and cardiovascular disease. Emerging data suggest that traditional cardiac risk factors, such as hyperlipidemia, diabetes, and obesity predispose patients to cancer as well. Indeed, obesity has been called the most important risk factor for cancer. At Vanderbilt, we are studying the underlying mechanisms and how specific interventions such as statins or exercise may reduce cardiovascular and cancer risk in the survivor population.

For additional information on the Vanderbilt Cardio-oncology Program, we encourage you to contact the author at: javid.moslehi@vanderbilt.edu.

References: