An update on your support of the Kaplan Cancer Research Fund

BY HENRY G. KAPLAN, M.D.

Last year donors like you gave nearly $1.5 million to support the Kaplan Cancer Research Fund (KCRF), giving our patients access to the newest, most promising research-based therapies to treat their cancer.

In particular, over the past year your investment made it possible for the Swedish Cancer Institute’s (SCI) Breast Cancer Group to continue work in some areas that have long been of interest, as well as some exciting new areas. Thank you for bringing hope and healing to countless people with cancer.

The registry that keeps on giving

The breast cancer registry at Swedish, which is supported entirely by philanthropy, continues to be one of the richest sources of data available to assist us in unraveling the changing patterns of breast cancer and how to treat it. What makes our registry stand out is that it contains complete, highly detailed data on our patients from diagnosis onward. In fact, our registry is so unique that one of my colleagues, David Beatty, M.D., and a team of researchers from the University of Washington are using it as the “gold standard” in their work to upgrade breast cancer databases throughout the nation.

Last year I told you we had used registry data to describe the behavioral differences between
breast cancers that are metastatic at diagnosis and those that are initially localized but subsequently spread and become metastatic. I am happy to report that this work has been published. For years researchers have lumped these two somewhat different cancers together in clinical trials, which may have skewed results and obscured potential findings. Based on our research findings, going forward we recommend that trials be targeted differently to help us better understand the metastatic process and how to treat it.

Digging deeper into the data, we were also thrilled to see that the outcomes for breast cancer treatment at Swedish far exceed those of other institutions in this region of the country! We have continued to document the improved survival of patients who have mammography-detected cancer. This has been quite dramatic for patients with inflammatory breast cancer.

And finally, our longtime registrar, Mary Atwood, recently announced that she plans to retire next year. Judith Malmgren, M.D., and I have been working with Mary on this project for almost 18 years, and though we will miss her, we’re confident that the registry is in very capable hands. Mary has designated Robinette Struckel—a registrar with an extraordinary background in tissue banking and forensic medicine—to assume her duties. Robinette, who has already been with us for some time, not only ensures the continuity of the group, but also brings additional dimensions and perspectives to what we are doing.

New treatments and new hope
On the treatment side, our group has continued to be very active in clinical trials. For nearly a decade we were members of the I-Spy-2 trial. This trial has studied a personalized-medicine approach to treating early stage breast cancer with new drug treatments. Last year Claire Buchanan, M.D., from our breast surgical group, and I participated in the development of I-Spy guidelines for the management of the armpit in patients who undergo surgery for their breast cancers.

In addition Erin Ellis, M.D., and I worked with the I-Spy group to coauthor a paper about a promising experimental drug called MK2206. The paper is currently being considered for publication at a prominent journal.

Last year marked our fifth year as a participating institution in the Academic Breast Cancer Consortium (ABRCC), which continues to be a source of exciting new research, including the following:

**Tucatinib/capcetabine**
The HER2Climb study has evaluated the use of this novel experimental drug, which appears to be very effective in the treatment of HER2/neu-positive breast cancer.

**Tucatinib/kadcyla**
As a result of the HER2Climb study’s success, Swedish has been invited as an individual institution to join a second trial that will combine tucatinib with kadcyla, another drug shown to be effective for patients with HER2/neu-positive breast cancer.

**Palbociclib**
In addition, we are supporting a study from ABRCC that is looking at adding a drug called palbociclib to standard chemotherapy and hormone therapy for HER2/neu-positive tumors. The consortium does not have enough funding to cover the cost of this study, but because we believe the drug may overcome resistance to standard therapy, we will rely on philanthropy to make up the shortfall.

We are also gearing up to participate in an ABRCC study that will attempt to guide preventive (adjuvant) hormone treatment by continually examining patients’ peripheral blood for fragments of circulating tumor DNA. If we see these fragments starting to appear, this suggests that the current treatment may not be effective, so we will switch adjuvant treatments without waiting for metastases to appear. We hope this will give us a head start on treating any resistant tumor cells present in the body.

Finally, philanthropy will fund an investigator-initiated study of a new treatment for patients who experience vaginal estrogen loss while undergoing hormone therapy for breast cancer. This has been a very difficult problem for a long time, so we are all very excited about launching this study, which will be spearheaded by Fenting Yan, M.D., and Kristine Rinn, M.D. We are in the final stages of writing the protocol—or roadmap—for the study and hope to activate it in the next few months.

**Expanding our reach**
Your support not only helps our patients; it also allows us to publish our research, which expands our reach. Sharing our findings with the broader medical community can augment—or even inspire—other research, while also making new treatments available to people outside of our hospital.

Breast cancer researchers have long debated to what degree lead-time bias has contributed to mammography-detected survival. To understand lead-time bias, consider a hypothetical patient whose cancer is detected at 40 and lives to 50. If her cancer was detected at 47 and she still lived to 50, is it fair to say that mammography prolonged her life?

This was the subject of a paper we presented at the San Antonio
Breast Cancer Symposium last December. For this paper we used data from our registry to look at all patients who developed metastatic disease, despite appropriate treatment, and to evaluate survival.

Indeed, the patients with mammography-detected tumors lived longer from diagnosis than those with tumors detected clinically, even though they eventually recurred. The time from recurrence to death was the same for both groups.

While this could suggest that the survival benefit from mammography is only the time from initial diagnosis to recurrence, it’s also possible that those who do recur despite timely diagnosis and appropriate treatment have something intrinsically different either in their tumors or the body’s response to the tumor and treatment. The next step will be to evaluate those tumors in greater detail, using genomics and other tools, to understand why they recurred.

In addition, we published papers in the following three areas:

**Chemotherapy and pregnancy**
Women of child-bearing age are at risk for both Hodgkin’s disease and breast cancer, making it important to minimize the risk that chemotherapy drugs present. Following up on our earlier work with the pharmacology group at the University of Washington on how pregnant women metabolize the drug doxorubicin, last year we published research on how the same population metabolizes dacarbazine.

**Chemotherapy and toxic bone marrow effects**
Alongside Greg Calip, Ph.D., of the University of Illinois, we further pursued our interest in bone marrow toxicity caused by chemotherapy on patients with breast cancer and the effect that bone marrow stimulants may have on the phenomenon.

**Malignant nerve sheath tumors**
I’ve reported before on our partnership with a commercial genomics company called Foundation Medicine to study malignant peripheral nerve sheath tumors. Last year we published an analysis of the genomic landscape of this uncommon tumor, which could help define one of the ways that cancer can occur from benign tissue, bringing us that much closer to a treatment.

**Looking ahead**
And then there are the projects that do not fit into any one category.

We continue to partner with Charles Cobbs, M.D., at the Swedish Neuroscience Institute, who has long studied the possible connection between a common virus called cytomegalovirus (CMV) and various forms of cancer. Together we have done preliminary work that has found evidence of this infection in breast cancer samples from our registry.

We are currently analyzing additional samples, and philanthropy has made it possible for us to bring on a highly regarded researcher from Sweden named Mohsen Karimi, Ph.D. He’s already hard at work, isolating genetic fragments of CMV in an attempt to better understand the role that CMV might play in the evolution of normal breast tissue to cancer.

Finally, along similar lines, we have just started a research project with another commercial genomics company to analyze changes in not only genes, but also RNA and the body’s immune response as breast tissue progresses from normal to precancerous to cancer.

For years we’ve focused breast cancer genomic research on mutations, without much success. Now, partnering with Anna Berry, M.D., who heads our genomics program, we’re shifting to take a more detailed look at how genes work and what factors may “turn on” cancerous growth.

Dr. Berry and I are also partnering with a company in the Netherlands for a study in which we will analyze the activity of multiple metabolic pathways before and after treatment with chemotherapy in an attempt to determine which pathways are important to the success or failure of the chemotherapy.

This has been yet another exciting year for our group, and we have you to thank. Without you and your support, none of this work would be possible. Thank you for your commitment to cancer research and our patients.

All the best,
Hank
“When I started in oncology, there were no decent treatments for breast cancer. Now we have, in certain situations, cure rates of 90 percent to 95 percent. That’s why I do this.” —HENRY G. KAPLAN, M.D.

SWEDISH BREAST CANCER REGISTRY BY THE NUMBERS

<table>
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<tr>
<th>29</th>
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<td>Years we’ve collected data</td>
<td>Cases added in 2018</td>
<td>Total cases in the registry</td>
<td>Patients still alive as of the last follow-up</td>
<td>Papers derived from data in the registry</td>
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Papers and Abstracts We Published Last Year

Publishing research allows us to help more patients in more places by making our findings available to everyone. And in the past year, the SCI Breast Cancer Group had the opportunity to publish several papers—many of which were born out of our Breast Cancer Registry.

Papers


Abstracts


Thank you for your extraordinary caring.

To continue your support of innovative and compassionate cancer care at Swedish, please contact:

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