Fighting Pediatric Cancer

he first time he was diagnosed with lymphoma at 15, Rabeh Ghadban wasn't too worried. His doctors in the pediatric hematology/oncology division at UCLA told him he had an 85 to 90 percent chance of surviving.

But when the cancer came barreling back only a month after he finished six rounds of grueling chemotherapy, the normally upbeat teen-ager was less confident about his chances.

"When my cancer came back so fast, it was the first time I felt this disease could take my life away," said Ghadban, now 19 and a student at the University of California, San Diego. "That was by far the toughest point for me. I didn't think for even one second that my cancer could come back, so when it came back, it was a huge surprise."

But Ghadban decided to trust his UCLA doctors and do all he could to fight the cancer. He underwent more grueling treatment and today he is cancer free. He's one of many success stories to emerge from the pediatric cancer program at UCLA—healthy teens and young adults pursuing their dreams now that their cancer experience is behind them.

It wasn't so long ago that a diagnosis of childhood cancer was considered a death sentence. Prior to 1970, most children and

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—DR. THEODORE MOORE shown at left with patient Kelly Mojica

young adults under 20 who were diagnosed with cancer had little hope of being cured.

Today, just three decades later—a virtual eye blink in the world of science—nearly 80 percent of all pediatric cancer patients have a chance of surviving to the five-year mark and beyond thanks to remarkable advances in treatment.

Dr. Stephen Feig saw this change firsthand. He came to UCLA in 1973 and became head of the pediatric hematology/oncology division in 1975.

"It's a total turnaround," Feig said, a professor of hematology/oncology who stepped down as division chief in July. "We've made major strides, and it has happened in a relatively short period of time."

hose in the pediatric cancer program at UCLA are working to push that 80 percent survival percentage upward even further.

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Most pediatric cancer patients are treated with chemotherapy, radiation or surgery—usually a combination of two of the three. UCLA pediatric oncologists are hoping to bring the new wave of cancer treatments—therapies that target the molecular abnormalities in tumor cells—to their young patients. And they're studying the late effects of cancer treatment that show up years and even decades later so they can determine how much therapy to give to pediatric cancer patients now so they suffer fewer treatment-related problems later on.

"We've really made a lot of progress in treating pediatric cancers," said Dr. Kathy Sakamoto, the new head of the pediatric hematology/oncology division. "But we still have challenges. The survival rates are not as good as they could be. We need to learn more about how to prevent relapse."

Sakamoto and pediatric oncologist Dr. Theodore Moore are teaming up to bring Phase I and II studies of molecularly targeted

therapies to pediatric patients. Sakamoto, a professor of hematology/oncology and pathology and laboratory medicine, will be doing preclinical studies in her lab on promising agents, testing them on pediatric cancer cells lines and then in animal models. Those agents that show efficacy will be tested in clinical trials run by Moore, an associate professor of hematology/oncology. They also hope to convince drug companies to test existing targeted therapies on pediatric patients.

Moore and Sakamoto face several hurdles. Pediatric cancers are rare—only about 12,000 new cases will be diagnosed in the United States this year. With so few patients as potential customers down the line, there is little financial incentive for drug companies to test new therapies on children. Also, with pediatric patients, who are still growing and developing, there may be toxicities from these experimental drugs that don't surface in adults.

ut the tide may be turning. A law passed in the late 1990s gives drug companies an additional six months of patent protected exclusivity if they include pediatric patients in their clinical trials—a financial enticement the pharmaceutical industry may need to make a policy change. And more and more pediatric oncologists, advocates like Moore and Sakamoto, are pushing for the study of targeted therapies in pediatric patients.

"There are more than 400 new anti-cancer agents in the pipeline now, and none are designed for children," Moore said. "It quickly became apparent that the only way to get those agents into pediatric clinical trials was to have excellent preclinical testing.'

If Sakamoto's preclinical testing shows that a particular agent works, that may help convince a drug company to test that therapy in the pediatric population, Moore said.

Also aiding the effort is the fact that about 50 percent of pediatric patients are already treated in clinical trials as compared to about 4 to 5 percent of adults. Why such a difference? The vast majority of pediatric patients are treated in academic medical centers that are part of a national cooperative working group —the Children's Oncology Group—where the best and most leadingedge therapies are available in clinical trials.

So the study infrastructure and patient population is in place. All that is needed are the agents to test.

"We want to be a leader in this area," said Moore, who hopes to have the first pediatric studies of targeted therapies open by early next year.

Moore and Dr. Linda Liau, an associate professor of neurology, recently received approval from the U.S. Food and Drug Administration to test a dendritic cell brain tumor vaccine in pediatric trials. An early phase UCLA study of the vaccine in adults conducted by Liau has shown significant promise.

The vaccine will be used to treat children with anaplastic astrocytoma and glioblastoma multiforme, particularly aggressive brain tumors for which there are no effective therapies, Moore said.

A second focus of the pediatric cancer program is studying the late effects of cancer treatment. Because more childhood cancer

patients are surviving into adulthood, there's a new population to study—a population at risk for serious physical and psychological problems as a result of their cancer treatment.

As many as two-thirds of the 270,000 childhood cancer survivors alive today are likely to experience at least one late effect, with about one-fourth experiencing a severe or life threatening complication.

Late effects include endocrine problems including growth and fertility issues, cardiac problems, learning disabilities, psychological dysfunction and second malignancies. Late effects can show up as many as 20 to 30 years after treatment.

he Life After Cancer Clinic at UCLA was created to serve this population. It follows pediatric and adult cancer survivors treated at UCLA as well as those referred by community physicians. Run by a team that includes an oncologist, a family nurse practitioner, clinical social workers and a school/vocational reintegration specialist, the program provides a comprehensive health evaluation, a psychosocial assessment and sub-specialty referrals. Survivors receive a thorough summary of all previous therapies they received and information on their risks for developing one or more late effect.

Feig said this area of study is vital, not only to the aid childhood cancer survivors, but to help shape the treatments that pediatric cancer patients are getting today.

"We need to learn more about what we're doing to these kids long term," he said. "This program will tell us what went wrong because of what we did right and how we can fix it."

Led by Dr. Jackie Casillas (see related story on page 17), the Life After Cancer Clinic fills a significant void in care. A recent study indicated that less than 50 percent of survivors of childhood cancer are getting the appropriate long-term follow-up care.

"There's a big segment of the survivor population that is lost to follow-up care," said Casillas, an assistant professor of pediatrics and a researcher in Cancer Prevention and Control Research at the Jonsson Cancer Center. "We hope to change that."

Ideally, childhood cancer survivors should be followed for life in a multidisciplinary program designed to monitor specifically for all known late effects, both physical and psychosocial, Casillas said.

"At UCLA, we've always followed our childhood cancer survivors," she said. "Now, we'll do so in a more systematic fashion. We'll provide a multidisciplinary approach to care, building our foundation on research."

Improving treatment and survival for children and adolescents with cancer remains the top goal for the pediatric cancer program.

"With all the progress we've made, we can offer patients and their parents some hope now," Sakamoto said.

It was that hope and the caring staff at UCLA that pulled survivor Rabeh Ghadban through some of his darkest hours, he said.

"The care I got was the best I could ask for. The staff is like a second family to me," Ghadban said. "I could tell they truly cared about me and were pulling for me. To have that much confidence in the people who had my life in their hands was definitely essential in keeping me strong and giving me peace of mind. I knew that everything that could be done was being done."