Spring 2015

FCS THE MAGAZINE

An Angel on a Mission

Pilot Elina Lunin

Image: Colored scanning electron micrograph (SEM) of a lung cancer cell.

One focus: a shared commitment to improve the lives of cancer patients everywhere.

We are excited to announce the launch of **TAKEDA ONCOLOGY** formerly known as **MILLENNIUM: THE TAKEDA ONCOLOGY COMPANY.** Our mission is unchanged as we endeavor to deliver extraordinary medicines to patients with cancer worldwide through our commitment to science, breakthrough innovation and passion for improving the lives of patients.

This singular focus drives our aspiration to discover breakthrough oncology therapies. By concentrating the power of leading scientific minds and the vast resources of a global pharmaceutical company, we are finding innovative ways to improve the treatment of cancer. We've built a portfolio of paradigm-changing therapies and a leading oncology pipeline. While we've made great strides in our fight against cancer, we are determined to do more—to work harder, to achieve greater—and to do it with the same passion, agility and entrepreneurial spirit that has always been at the heart of our culture and made us the leaders in oncology that we are today.

We know that our mission is not a quick or easy one but we are up to the task: we aspire to cure cancer.

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A message from

Brad Prechtl

The new year is underway! Now into 2015, it's important to reflect on what we accomplished over the past year and prepare for the continuing changes that are anticipated in the health care industry.

Despite some major challenges in 2014, we enjoyed a successful year and celebrated our 30th anniversary, added 11 new office locations and 19 new physicians to the practice, expanded into two new counties and experienced several firsts, including establishing our first exclusive agreement with Florida Hospital in Flagler and Volusia counties and completing our first exclusive managed care agreement with the FHHS Volusia/Flagler hospital employees.

I am delighted to report that through the continuation of our Operational Excellence Program, we identified significant savings and improvements in the areas of overtime management, radiology leakage, ambulatory pump management and pharmacy charge capture projects. Also in 2014, new and/or major renovation projects commenced for Brandon, Broadway, Clearwater, Clermont, Hudson, Leesburg, Medical Park, Ocala, Paylor, The Villages and the initial phases of the Rx to Go corporate expansion. We also expanded our hematopathology services with the addition of FISH technical testing.

Our management team continues to identify ways to improve outcomes, reduce costs and demonstrate value to YOU—our stakeholders. FCS strives to set new benchmarks for community oncology and further define its role as an innovator in the health care industry, both clinically and from a business perspective.

I am inspired daily by the dedication to our patients that I observe from all our physicians, nurses and team members. I am extremely proud and privileged to serve this organization. As we prepare for the next year of evolution, I look forward to working with each of you and anticipate another successful year for our practice.

Brad Prechtl
Chief Executive Officer

in this issue

DEPARTMENTS

SPOTLIGHT

FEATURE

ARIAD

An Interview with Marty Duvall, Executive Vice President and Chief Commercial Officer

ARIAD Pharmaceuticals, Inc., headquartered in Cambridge, Mass., and Lausanne, Switzerland, is an integrated global oncology company focused on transforming the lives of cancer patients with breakthrough medicines. ARIAD is working on new medicines to advance the treatment of various forms of chronic and acute leukemia, lung cancer, and other difficult-to-treat cancers. ARIAD utilizes computational and structural approaches to design small-molecule drugs that overcome resistance to existing cancer medicines.

Marty Duvall

Q: Can you describe ARIAD's approach to drug discovery and development?

Our mission is to discover, develop, and commercialize small-molecule medicines to treat cancer in patients with the greatest unmet medical need—those with aggressive cancers where current therapies are inadequate. We are committed to the highest standards of integrity and stewardship in service to patients, the medical community, employees, and shareholders.

While the company has been focused on research and development (R&D) for the past 20 years, we're new to commercialization. Our team is fully fueled and delivering our first drug to patients. We've gone through quite a revolution as a company in the last 24 months—which drives us more and more every day.

Q: What can you tell us about the origin of the company's unique name, ARIAD?

It's a good story. The name ARIAD originates from the Greek myth of Ariadne, a daughter of Minos II, king of Crete. According to the myth, Ariadne fell in love with Theseus, the founder-king of Athens, and gave him a spool of thread that enabled him to trace his path safely in and out of the labyrinth in which the Minotaur lived. After slaying the Minotaur, Theseus used the spool of thread to return home.

At ARIAD, we see a powerful connection between this ageless story and our vision—the labyrinth symbolizes the complex system of molecular pathways within the cell, and the spool of thread represents the pathways that are leading our scientists to the discovery of breakthrough cancer medicines.

Q: How would you describe ARIAD's evolution as a company transitioning from an R&D shop to a fully commercial organization?

Our CEO, Dr. Harvey Berger, founded ARIAD in the early 1990s with the idea—thought virtually impossible at the time—that the right drug could find its way safely through the labyrinth of molecular-communication pathways and destroy a disease from within. He and the company's collaborators helped map out an alternative way of discovering drugs, focused not on screening millions of compounds, but using cutting-edge computational technology to understand the structure of molecular targets and attack them in the most effective and efficient way possible.

Twenty years later, we are working to build off that legacy. The fact is we are now a vibrant, growing pharmaceutical company with a focus on oncology. This is the ARIAD we see. This is how we're making that vision a reality: by attracting, developing, and retaining the best and brightest minds—building upon our solid team of people, seeking individuals from diverse backgrounds in drug discovery, development and commercialization, financial management, and business strategy. I'm proud to work with some of the best and brightest in this industry.

In those efforts, we leverage ARIAD's strengths—scientific excellence and clinical scholarship—to broadly develop our lead oncology product candidates and build a pipeline of innovative follow-on product candidates. This allows us to build a world-class commercial organization to bring our new medicines to cancer patients on a global basis.

Q: Have you encountered any significant challenges during ARIAD's transition to commercialization?

Yes, unexpected challenges are par for the course for any biotech striving to make the leap to a fully operational commercial company, and our journey is no different. But, in a lot of ways, our biggest challenge this past year has led to the commercial team's proudest moments.

Quick background: In early 2013, we celebrated the successful launches of our first approved medicine in the U.S. and EU. Following a successful eight-month commercial run in those markets, our product was temporarily pulled from the U.S. market at the end of 2013 so that ARIAD and the regulatory agencies could work together to evaluate safety signals. The six-week halt to our commercial efforts was unexpected, but with the issuance of revised labeling and a safety plan in collaboration with the health authorities in the interim, we resumed commercial efforts. Critical to those efforts, we're committed to ongoing studies and informing healthcare providers about the risk-benefit profile of our product.

During the six-week suspension of commercial activities in the U.S., and in conjunction with the FDA, we continued to meet physician requests for our product through a single-patient Investigational New Drug (IND) program; through this program, qualifying patients received the product at no cost. I'm proud of that. In addition, we received an unsolicited but overwhelming outpouring of support from the patient and physician communities. That outpouring inspired, sustained, and reminded us of the significance of our work, particularly during a difficult time. We remain forever grateful to those communities.

And, I'm incredibly proud of our commercial team for coming together to help overcome what was easily the most precarious time in our short commercial history. I am blessed with the most talented, experienced, and collegial team in this industry, who are motivated every day by an uncompromising commitment to our patients.

Q: Can you speak to your product pipeline?

We continue to investigate other resistant forms of cancer for our lead product, and are currently enrolling patients in a study looking at gastro-intestinal stromal tumors

(GIST). Additionally, we have numerous investigator-sponsored trials (ISTs).

We are exploring a second targeted cancer therapy in anaplastic lymphoma kinase (ALK) positive non-small cell lung cancer (NSCLC) and, in fact, have recently received Breakthrough Therapy Designation from the FDA and are currently enrolling patients in a phase two registrational trial.

Q: Do you feel ARIAD can compete with larger pharmaceutical Goliaths in the industry? How so?

The fact is, the old model is changing and a smaller, more nimble, more focused organization has its advantages. We have a cohesive group of entrepreneurial-minded people, who have worked in the silos of big pharma and have chosen ARIAD's mission as their own. Our team, while quite small, is able to move quickly with our customers and patients in mind. They're passionate about what we do for our very specific patient population and it shows in every interaction they have.

Q: What programs does ARIAD have in place to provide value to the community oncology setting?

We're committed to supporting community oncologists because they are a cornerstone in the care for most cancer patients. ARIAD has been a sponsor and participant at most ION Solutions physician and administrator meetings since January 2013. We sincerely value the advice of community oncology physicians. We have conducted focus groups to gain the perspective of how our drug and our team can best meet their patients' needs. ARIAD also is involved in sponsoring ION In-Practice Programs when practices are interested in having a disease expert come to their practice location to present clinical information in support of patient care. Finally, through ARIAD PASS we offer important reimbursement programs for chronic myeloid leukemia (CML) patients so that when a physician prescribes our drug, they have the ability to get the drug even if they cannot afford the co-pays or have no insurance. The ARIAD sales and marketing teams recognize the need to continually bring value in their interactions with community oncology practices and we are committed to doing so.

Q: 10 years from now, what do you hope to be able to say about ARIAD's contribution to cancer care?

I think in 10 years we'll be able to say that we've delivered on our vision to transform the lives of cancer patients. We have two cancer compounds on which we will have been able to collect more data, and, most importantly will have helped patients in their fight against their disease. We have more work to do in these next 10 years, to fully establish ourselves globally. I also see ARIAD playing an important role in providing education for understanding genetic markers in cancer progression.

Q: How is ARIAD focused on helping patients?

This is in everything we do. From the initial conception of our drugs to our patient programs, we're looking to help patients who have run out of treatment options. We're committed to our patients. As I mentioned above, during last year's events we worked around the clock to make sure that patients who needed it were able to obtain it through special applications to the FDA. Our teams from regulatory, manufacturing, advocacy, medical information, and others banded together for this purpose and we're proud that we were able to meet the need of our patients, some of whom we've gotten to know personally. Knowing we helped them and their families means the world to us.

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Pilot Elina Lunin is an Angel on a Mission

BY ZANDRA WOLFGRAM

It's official. Elina Lunin is an angel… and she has the wings to prove it. For the past year, the 41-year-old certified pilot/instructor has been on the official roster for Angel Flight Southeast—a nonprofit organization made up of 650 volunteer pilots who donate their time, fuel and use of their own aircraft to provide free air transportation for medical patients in need throughout Florida.

Her first mission was on a spring day in March 2014. She was to fly a 30-year-old female patient who was nearing the end of 10 years of treatment from Punta Gorda to Fernandina Beach. As Lunin recalls, the patient had a great mental attitude but was too physically weak to make the drive by car. What should have been a fairly quick flight took three hours as Lunin was forced to navigate Geronimo, her Piper PA-23, around bad weather. Still not bad considering that by car it would have been a five-plus-hour drive.

That flight was not only convenient, but apparently the experience in itself was inspiring to the young woman.

"She asked me for my business card and told me, 'When I am well, I am going to save up to take flying lessons,'" Lunin recalls.

Since that first flight, Lunin has relocated to Sarasota with Geronimo, and is now officially registered there. The effervescent brunette loves the beautiful and bustling area, which offers so much for her family to do. And because it is a larger city, she has been thrilled to see even more Angel Flight missions pop up in her email.

Just like her inaugural "discovery flight" in 2009, once she was airborne with her first patient, this easygoing gal was hooked.

"I totally loved it. I just think it's a wonderful thing to do," Lunin says.

Altogether, she has volunteered her time and plane for 10 missions. At the urging of Angel Flight, Lunin makes it a point to snap a keepsake photo with each of her passengers, except one—an emergency flight to the East coast for a woman in her early 50s recovering from a bone marrow biopsy.

"She was just too ill to be taking a picture, and in that moment I learned to really pay attention and respect how my passengers are feeling," Lunin shares.

Though transporting sick patients in need can be difficult, Lunin realizes it's much more so for those she ferries.

"When you think about it, it takes courage to get into a small plane," she says. "Not everyone can do it. These patients not only have courage to undergo treatment but also to get into a small plane. I admire them."

Patients aren't the only ones appreciative of the service. Dr. Manish Patel, who oversees the Early Phase Clinical Trial research program in Sarasota for Florida Cancer Specialists & Research Institute, began using Angel Flight two years ago for some of his patients participating in clinical trials.

"About 50 percent of our patients come from outside of a 90-minute drive," he says. "Most drive, but there are a good number who fly on their own and pay out of pocket. Not everyone can afford it, so there are some who are happy they can use the Angel Flight service."

Patel currently has about 10 patients who have relied on the service to continue care.

"It really reflects the compassion that we have in oncology to offer this service," he says. "Patients who are having good responses love the service because they are able to continue their trials and get access to drugs when living far away."

Flying isn't something Lunin takes for granted. Born in Argentina, she admired her father, who was an air force officer there.

"I was always intrigued by flying and airplanes but not sure I could do it," she says. Back home, women were not allowed to enter the armed forces and therefore were not exactly encouraged to fly, so she was elated to be able to pursue lessons while living in Punta Gorda—where she lived for 12 years before moving to Sarasota last summer. "You don't have general aviation everywhere as you do here in the U.S. I feel so lucky to be able to do it."

And how did she feel the day she earned her wings?

"It was a dream," she says. The more she flew, the more she loved it. She says she celebrates each and every rating. Today, Lunin is proud to have earned a certified pilot's rating for single-engine and multi-engine planes and instruments.

For Lunin, serving people through Angel Flight is an opportunity for her to pay her personal debt of gratitude forward.

Some of Dr. Manish Patel's patients have participated in clinical trials thanks to angels like Elina Lunin.

"There's nothing better for me to do than to give back, because I feel so lucky and so blessed."

Among the blessings she counts is her 20-year marriage to Scott Lunin, M.D., who practices oncology out of FCS' Sarasota office, and their two children, Isabella, 14, and Michael, 11.

But don't count on the Lunin family to appear on Geronimo's manifest list anytime soon.

"They don't like flying," Lunin laments with a laugh. "I don't push it, but that is one of my goals, to fly my family to a vacation one of these days."

For Lunin, it's hard to imagine any greater joy than flying. It's obvious there is nowhere she'd rather be than up in the air.

"It's freedom. It's peaceful. It's beautiful," she says. "And you certainly see things from a different perspective."

And thanks to caring Angel Flight pilots like Lunin located all over the U. S., more than 3,000 grateful patients a year are sure to have a much healthier perspective on life, too.

Did You Know?

Angel Flight started in 1983 in California.

Florida belongs to the Angel Flight Southeast wing. It is a member of Air Charity Network, an association of charitable aviation organizations composed of more than 7,000 pilots who have flown more than 22,000 missions for 35,000 passengers nationwide since 2006.

Angel Flight Southeast coordinates missions to fly organ transplant candidates; people involved in clinical trials, chemotherapy or other repetitive treatment; victims of abuse seeking relocation; families receiving help from Ronald McDonald Houses, Shriners Hospitals and many other charities; disabled or sick children attending special summer camp programs; and for many other humanitarian reasons.

Who is Eligible?

Angel Flight Southeast is not an air ambulance or on-demand service. Patients must be medically stable, ambulatory and capable of sitting upright and wearing a seat belt for the duration of the flight. There must be either a demonstrated financial need or reason why public transportation cannot be utilized.

Patients must be able to be transported in an unpressurized aircraft. The treatment they are seeking must be conventional or authorized investigation protocols that are not available locally, or Angel Flight Southeast will transport the patient when local treatment is not working. A doctor's medical release will always be required prior to flight.

How to Reserve a Flight

Be sure to check the Patient Guidelines located online at angelflightse.org.

Allow for at least two weeks' notice when arranging an Online Flight Request.

The Angel Flight staff will review your request and follow up with you to complete any additional requirements.

Since bad weather could prevent pilots from flying a mission, all passengers must have a backup plan.

Social workers and/or physicians may call the Mission Request Hotline Monday through Friday, 8:30 a.m. to 5 p.m. Eastern time, at (800) 352-4256.

How to Become an 'Angel'

Pilots are always welcome to join and participate, but you don't have be a pilot to "earn your wings" with Angel Flight.

There are numerous opportunities for "Earth Angel" volunteers. At the headquarters in Leesburg, Florida, volunteers answer phones, coordinate missions and accomplish other vital office-related tasks.

Throughout Florida, Earth Angels take on coordination and other duties at the various Wing chapters. For more information about how you can become more involved with Angel Flight, visit angelflightse.org.

Angel Flight is supported through individual contributions. If you don't have the time to give but would like to make a contribution, visit the Sponsors page online. Angel Flight takes no government funding. It relies on community support. For every dollar of direct public support, it returns $5 of service to the community. You can make a tax-deductible contribution to Angel Flight Southeast with just a click by visiting angelflightse.org.

Take Part!

Angel Flight hosts special fundraising events year-round. To participate in one near you, check out the calendar listing online at angelflightse.org/events.

Foundation Medicine:

Transforming Cancer Care

Foundation Medicine is a molecular information company dedicated to a transformation in cancer care where treatment is informed by a deep understanding of the genomic changes that contribute to each patient's unique cancer.

FCS recently spoke with Dave Daly, Foundation Medicine's chief commercial officer, about how comprehensive genomic profiling and targeted cancer therapies are enhancing patient care.

Q: How is Foundation Medicine enhancing care for cancer patients?

Foundation Medicine makes precision medicine a reality for patients by offering comprehensive genomic profiling to oncologists. Our clinical products, FoundationOne and FoundationOne Heme, identify the genomic alterations unique to each patient's tumor and match them to targeted therapy or clinical trial options to support oncologists in identifying treatment options for their patients that may not have otherwise been considered. The results of our tests are provided in an easy-to-read interpretive report with the relevant alterations in a patient's tumor and the latest medical and scientific findings to support physician treatment recommendations. Foundation Medicine also collaborates with leading drug developers and cancer researchers to identify novel targets and redesign clinical trials to accelerate the development of targeted cancer therapies and continue to push the field of cancer care forward, bringing new therapies to patients faster.

Q: Foundation Medicine markets two clinical products: FoundationOne® and FoundationOne® Heme. Please explain these tests.

FoundationOne and FoundationOne Heme are fully informative and comprehensive genomic profiles that complement traditional cancer treatment decision tools and often expand treatment options by matching each patient with targeted therapies and clinical trials that are relevant to the molecular changes in their tumor. Our comprehensive genomic profiles differ fundamentally from other next-generation sequencing (NGS) based genomic testing for cancer by analyzing the entire coding regions of the genes of interest and detecting all classes of genomic alterations at an exquisite level of accuracy, only achievable by our hybrid capture-based sequencing method.

The hybrid capture-based sequencing method permits the quantification of the number of unique input DNA molecules to ensure a high level of sensitivity and specificity when detecting genomic alterations in every specimen. Our clinical products have undergone robust analytic validation, the first to

FOUNDATION MEDICINE®

be published in a prestigious peer-reviewed scientific journal, and can be performed on routine cancer specimens, such as FFPE samples, and in the case of FoundationOne Heme, peripheral blood or bone marrow samples. The test results are provided in easy-to-read reports with the most clinically relevant information to help inform patient treatment.

FoundationOne, Foundation Medicine's product for solid tumors, utilizes next-generation sequencing to interrogate the entire coding sequence of 315 cancer-related genes plus select introns from 28 genes often rearranged or altered in solid tumor cancers. These genes are sequenced to identify all classes of clinically relevant somatic alterations, including base pair substitutions, insertions and deletions, copy number alterations, and select rearrangements.

FoundationOne Heme, Foundation Medicine's product for hematologic malignancies, sarcomas and pediatric cancers, uses next-generation sequencing (NGS) to assess the coding regions of 405 cancer-related genes through DNA sequencing and 265 genes through RNA sequencing to capture a broad range of gene fusions. FoundationOne Heme simultaneously detects all classes of genomic alterations, including base pair substitutions, insertions and deletions, copy number alterations and select rearrangements, including fusions.

Q: Explain how Foundation Medicine collaborates with pharmaceutical manufacturers.

Foundation Medicine collaborates with more than 20 biopharmaceutical companies and many more academic medical centers to identify novel targets and accelerate the development of targeted cancer therapies. Our molecular information platform enables our partners to more quickly select promising drug candidates and to identify genomic signatures and mechanisms of sensitivity or resistance. In turn, this information is used to design more efficient clinical trials to accelerate the delivery of safe, effective targeted therapies for patients with cancer.

Q: Does Foundation Medicine participate in clinical trials?

Foundation Medicine actively collaborates with both drug developers and research centers on a variety of clinical trials. In 2014, the company was involved in more than 100 clinical trials with biopharmaceutical and academic research partners. Foundation Medicine's platform also was selected to be used in the Lung-MAP trial, a multi-stakeholder collaboration between biopharmaceutical companies, patient advocacy groups and foundations and Foundation Medicine.

Q: How does a practice order FoundationOne or FoundationOne Heme for a patient?

FoundationOne or FoundationOne Heme can be ordered by a physician by completing a test requisition form, which can be found on FoundationOne.com. A physician's office only needs to complete the requisition form and Foundation Medicine will contact pathology to obtain the sample.

For FFPE specimens, Foundation Medicine will procure the specimen from pathology and return an easy-to-read interpretive report within 14 days of sample receipt for FoundationOne and 18 days for FoundationOne Heme. For blood and bone marrow aspirates, the physician can

send the specimen with the test requisition and we begin processing as soon as the sample arrives at our laboratory.

Q: What programs does Foundation Medicine have in place to provide value to the community oncology setting?

Both FoundationOne and FoundationOne Heme were designed to bring clinically relevant developments in cancer biology to patients everywhere, including in the community oncology setting. Both tests can be performed on routine cancer specimens and easy-to-read interpretive reports are delivered to oncologists within 14 days of sample receipt for FoundationOne and within 18 days for FoundationOne Heme.

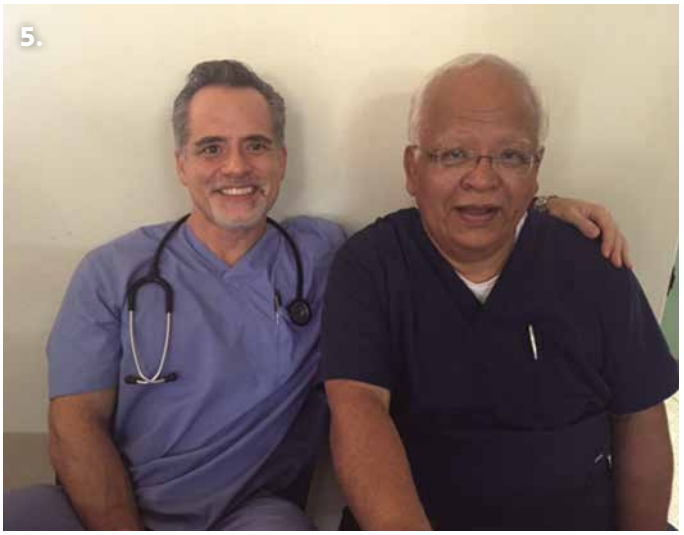
Our Client Services and Medical Affairs team help provide information and guidance on interpretation of results and a seasoned team of account executives can provide clinical and logistical support. Foundation Medicine also offers educational programming by way of webinars, molecular tumor boards and speaker programs to educate practices on how to utilize comprehensive genomic profiling. If a physician has a promising patient case they would like to share with a broader audience, we are happy to assist in reviewing and potentially publishing compelling clinical narratives that demonstrate the impact of precision medicine in oncology.

To support patient-centric care, Foundation Medicine offers patient education materials to help patients understand comprehensive genomic profiling and is dedicated to reducing financial barriers that may keep patients from benefitting from our products. We offer a financial assistance program to help patients navigate the insurance billing process and reduce the out-of-pocket costs for FoundationOne and FoundationOne Heme.

Beyond our direct services, Foundation Medicine partners with leading service providers to help patients benefit from our products. The FoundationOne CareLine helps patients access any relevant targeted therapies identified by our tests and selected by oncologists as an appropriate treatment option. Through FoundationOne CareLine, patients are assigned an individual case manager from our partner, the Patient Advocate Foundation, to navigate the reimbursement process, appeal for coverage on the patient's behalf or secure compassionate use. Through our partnership with EmergingMed, Foundation Medicine offers clinical trial navigation services to conduct a thorough search of relevant clinical trials matched to a patient's clinical and genomic profile and to assist in enrollment on trials selected by the oncologist and patient.

> "Foundation Medicine collaborates with leading drug developers and cancer researchers to identify novel targets and redesign clinical trials to accelerate the development of targeted cancer therapies and continue to push the field of cancer care forward, bringing new therapies to patients faster.

Foundation Medicine also aims to improve patient care through novel technology products such as our Interactive Cancer Explorer® (ICE). The newest version of this product, ICE 2, includes features that increase the efficiency of patient care and a new approach to enhancing the ability for physicians to act on the results of our comprehensive genomic profiles: PatientMatch™. PatientMatch connects physicians with shared experiences treating patients with similar genomic profiles to inform their treatment decisions.



1. Yankees vs. Pirates' Spring Training Game: CEO Brad Prechtl throws out first pitch.

2. Women of Interest Conference, Tallahassee, sponsored by FCS: Pictured (L to R): Deb Mabry, Tallahassee Offices Manager; Elmira Mangum, Ph.D. and President of Florida A&M University; Shelly Glenn, Chief Marketing & Sales Officer; and Sandra Brooks, Physician Liaison, Tallahassee.

3. SCRI Scientific Meeting, Nashville, TN (Feb. 6, 2015): Pictured (L to R): Dr. Fadi Kayali, Dr. Gail Wright, Dr. Jim Reeves, Katie Goodman, Dr. Bill Harwin, Dr. Paresh Patel, Dr. Lowell Hart, Dr. Andres Soriano, Dr. Manish Patel.

4. Run Amuck with the Duck 4K Event: Pictured (L to R): Ricky Bennett, Angela Cotman, Janice Brown, Becky Mooneyhan, Holli Smith, Sandy Brooks, Clyde The Bulldog, Shanedra Gordan, Kathy Connery, Dr. Lucio Gordan, Julia Gordan (Dr. Gordan's daughter).

5. Dr. Michael Diaz and father on Jamaica Medical Mission: The father-son team saw 732 patients, filled almost 2,000 prescriptions and fitted over 200 with reading glasses.

6. Opening day for new volunteer program at GSF Flagler for FCS Foundation, West Palm Beach (Feb. 16, 2015): Top (L to R): Naomi Poston, Head Nurse, and Lois Udell, Volunteer. Above (L to R): Naomi Poston, Head Nurse; Lois Udell, Volunteer; and Valerie Vance, FCS Foundation Volunteer Program Manager.

7. Integrative Oncology Open House (Nov. 15, 2015): Dr. Jooma juicing at the Highland Office First Integrative Oncology Open House..

8. Annual Christmas Tree Giveaway: Pictured (L to R): Andrea Bolivar, Highland Office Manager; Dr. Kerry Chamberlain; Andrea Forster.

9. Suncoast Leukemia & Lymphoma Society's 2015 Man/Woman of Year launch (Mar. 5, 2015): Nominating Committee along with 2014 winners, Dr. Gregoire Bergier and Shelly Glenn, Chief Marketing & Sales Officer.

10. Integrative Oncology Program Open House (Nov. 15, 2015): Dr. Jose Alemar speaking to open house attendees at the Highland Office.

11. Sari Center 5K Survivors Run, West Palm Beach Region 9: Pictured (L to R): Rachel Green, Dr. Bobby Green, Dr. Shachar Peles, Danielle Peles.

12. Florida Trust ACO (Feb. 17, 2015): Physician Liaison Rhonda Webster and several area FCS physicians attended the Florida Trust Accountable Care Organization (ACO) conference in Orlando.

13. CME Dinner Series, Brooksvile (Dec. 4 2014): Pictured (L to R): 'Immunotherapy In Cancer' speaker Dr. Evan Lipson from Johns Hopkins Kimmel Cancer Center & Sibley Memorial Hospital and FCS moderator Dr. Vikas Malhotra.

14. Twins? What are the chances?: Physician Liaison Manager Maria Ramos-Person and Dr. Richard Knipe.

Welcome Dr. Anjan Patel, Dr. William Harrer, Dr. Servillano Dela Cruz Jr., Dr. Noor Merchant and Dr. Raul Storey-Rojas

We welcome Dr. Anjan Patel, Dr. William Harrer and Dr. Servillano Dela Cruz Jr. of Citrus Oncology, Dr. Noor Merchant and Dr. Raul Storey-Rojas to the Florida Cancer Specialists & Research Institute organization.

As the newest physician partners at FCS, we are thrilled to have physicians of this stature join the FCS organization.


Patel

Dr. Patel earned his medical degree from Florida State University in Tallahassee, Florida, and his residency at Georgetown University Hospital/Washington Hospital Center in Washington, D.C. He completed his fellowship in hematology/oncology at The University of Florida in Gainesville, Florida.

Drs. Harrer and Dela Cruz will be practicing at their offices in Crystal River and Inverness, while Drs. Merchant and Storey-Rojas have offices in Vero Beach and Sebastian.


Dela Cruz

Dr. Dela Cruz Jr. has been practicing in Citrus County, Florida, since 2000 and provides physician leadership at Citrus Memorial Hospital in Inverness and Seven Rivers Community Hospital in Crystal River, both in Florida. He completed his Fellowship in Hematology/Oncology at Lenox Hill Hospital, New York University Medical Center and Mt. Sinai Medical Center in New York, New York.


Harrer

Dr. Harrer completed his Fellowship in Hematology/Oncology at Cooper University Medical Center in Camden, New Jersey, and practiced in Brunswick and Thomasville, Georgia, where he served as the Director of Medical Oncology and the Medical Director of Hospice at the Lewis Hall Singletary Oncology Center until 2001.


Merchant

Dr. Merchant completed a Fellowship in Oncology/Hematology at Wadley Cancer Research Center in Dallas, Texas, as well as a Fellowship in Medical Oncology at the University of Texas, MD Anderson Cancer Center in Houston.


Storey-Rojas

Dr. Storey-Rojas served as the Research Project Coordinator for an oncology group in Houston, Texas. During his residency and fellowship, he gained experience with the MD Anderson Cancer Center Bone Marrow Transplantation and Cellular Therapy Department.

Congratulations to Dr. Fadi Kayali and Dr. Marays Veliz

Join us in congratulating Drs. Fadi Kayali and Marays Veliz, who have become partners at FCS.


Kayali

Dr. Kayali earned his medical degree from St. Petersburg I.P. Pavlov Medical State University in Saint Petersburg, Russia, and completed his internship and residency at St. Joseph Oakland Hospital in Pontiac, Michigan. He received his fellowship at University of Louisville in Louisville, Kentucky, and is fluent in Russian, Arabic and English. Dr. Kayali practices at the Sarasota Cattlemen office.


Veliz

Dr. Veliz attended medical school at Instituto Superior de Ciencias Medicas de La Habana in Havana, Cuba. After completing her internship and residency at the University of Medicine and Dentistry in Newark, New Jersey, she received her fellowship at the University of South Florida, Moffitt Cancer Center.

New Office Relocation in Hudson

Florida Cancer Specialists & Research Institute opened a new clinical location in Hudson, Florida, on Jan. 10. Drs. Gajanan Kulkarni and Kapisthalem Kumar will continue the same clinical hours at this location, assuring there will be no interruption in patient care.

Ocala Office Welcomes Dr. Imad El-Jassous as it Undergoes Expansion and Improvement

Dr. Imad El-Jassous received his medical degree from the Lebanese University-Faculty of Medical School in Beirut, Lebanon. He then completed his residency and fellowship in hematology and oncology at the Staten Island University Hospital in Staten Island, New York.


El-Jassous

In addition to El-Jassous joining the office, FCS is expanding and improving the location by increasing the number of chemotherapy chairs in the infusion area to 18, enlarging the waiting room and pharmacy areas, adding a new lab with two chairs and doubling the number of exam rooms to provide six rooms for patient visits. With these improvements, the Ocala office will be able to offer more convenience to patients in the area.

New Office Location in New Smyrna Beach

FCS opened a new clinical location on Jan. 5 in New Smyrna Beach, Florida. Drs. Karin Bigman, Kathleen Doughney, Eric Harris and Mudussara Khan will be seeing patients at the new location.


Doughney

Dr. Ana Van Der Wall Joins Bradenton West Office


Van Der Wall

Dr. Van Der Wall began her career as a research associate and worked for two prestigious research laboratories in Carlsbad and Irvine, California. Her area of specialization focused on genetic research with breast cancer and tumors of unknown origin. She then continued her education and training in oncology/hematology and served as Chief Resident in Internal Medicine at East Tennessee State University in Johnson City, Tennessee. She has given numerous scientific presentations on such topics as Pancreatic Cancer, Multiple Myeloma and Non-Small Cell Lung Cancer. Fluent in English and Spanish, she has also been published in Cancer Cell, the peer-reviewed journal.

Groundbreaking Ceremony Celebrates $2.5 Million Expansion of Corporate Headquarters to Accommodate Growth

The expansion announcement was accompanied by a groundbreaking ceremony attended by FCS leaders and community officials, including Fort Myers Mayor Randy Henderson. Recognized as the leading community oncology practice in Florida, the company will add 21,132 square feet in the two-story build out set to be completed in 2015. Half of the new space will be used for administrative services; the other half will house an expanded Rx to Go program.


A groundbreaking ceremony for the expansion of the Florida Cancer Specialists corporate headquarters was held on December 1, 2014. In attendance at the event were Florida Cancer Specialists leaders and community officials, including Ft. Myers Mayor Randy Henderson.

Drs. Karin Bigman, Eric Harris and Mudussara Khan Join FCS at New Offices in Daytona and Ormond Beach


Bigman

A new FCS partner, Dr. Karin Bigman began her practice at the Comprehensive Cancer Center at Florida Hospital Memorial Medical Center in 1995. She has a keen interest in clinical trial research and has been a principal investigator and sub-investigator in multiple oncology/hematology research trials. She is a graduate of Mount Sinai School of Medicine, New York, New York, where she also completed her residency. Dr. Bigman earned a Fellowship in Oncology/Hematology at New York Medical College in Valhalla, New York.


Harris

Dr. Eric Harris received diverse preparation in his early medical training, having worked as a laboratory technician, research technician and medical technologist at Albany Medical Center in Albany, New York. He served as Chief Fellow, Hematology/Oncology at the University of Florida, Department of Medicine. Dr. Harris is also on the FLASCO Board.


Kahn

Dr. Mudussara Khan is board certified in Hematology, Medical Oncology and Internal Medicine. During her residency and fellowship at West Virginia University School of Medicine, Dr. Khan was recognized with several honors, including being named Chief Resident, as well as Chief Fellow, for the Department of Internal Medicine.

Dr. Wasif Riaz Joins FCS


Riaz

A graduate of Nishtar Medical College, Dr.Wasif Riaz completed his residency in Internal Medicine at Guthrie/Robert Packer Hospital in Sayre, Pennsylvania, and the University at Buffalo in Buffalo, New York. He was awarded a Fellowship in Hematology/Oncology at The University of South Florida/Moffitt Cancer Center in Tampa.

Party Under the Stars Raises over $50,000 for Florida Cancer Specialists Foundation

The Fiesta Bajo Las Estrellas (Party Under the Stars) benefit for Florida Cancer Specialists Foundation raised over $54,000. The second annual event was held Nov.

Mariachi band and festive dancers served as the entertainment for Fiesta Bajo Las Estrellas, a fund-raising event held in Sarasota to support non-medical living expenses of qualified cancer patients who are currently undergoing treatment in Florida.

15, 2014, at the Center for Building Hope. Foundation Board Chair Brad Prechtl and his wife, Terri, kicked off the festivities with a VIP reception at their home. The money raised goes to support the non-medical living expenses of qualified cancer patients who are currently undergoing treatment in Florida.

FCS Integrative Oncology Program Researches Use of Acupuncture for Chemotherapy-Induced Peripheral Neuropathy

The Integrative Oncology Program blends traditional oncology treatments with evidence-based complementary therapies, such as acupuncture, nutrition and yoga, to reduce some of the side effects patients may experience with chemotherapy or radiation. In collaboration with the University of South Florida , the Integrative Oncology Program, which is under the medical direction of Nuruddin Jooma, MD, MPH, and Integrative Oncology Coordinator Sarah Boses, RN, BSN, conducted a study evaluating the use of acupuncture for chemotherapy-induced peripheral neuropathy, an often-debilitating side effect of chemotherapy.

Acupuncture physician Dr. Gene Healy treats a patient at Florida Cancer Specialists.

Tampa Cancer Center

Tampa Cancer Center Introduces Prone Breast Radiation Treatment

This unique approach to the treatment of breast cancer has been shown to benefit patients in a number of ways, including sparing critical organs such as the heart and lungs from receiving excess radiation, which could later result in heart or lung disease.

The majority of patients with early-stage breast cancer are now treated with breast conservation therapy, such as a lumpectomy, followed by whole-breast radiation, which has typically been delivered with the patient in the supine position (lying on her back). Putting women in the prone position (lying face down) on a special padded treatment board allows the breast to hang freely and increases the separation of the breast being treated from the chest wall, thereby reducing radiation exposure to the heart and lungs.

Studies have shown that prone breast radiation substantially reduces exposure to the heart and lungs and may possibly improve the short and long term effects of radiation on the treated skin. In addition, the prone position can help reduce respiratory motion, which allows more uniform dose delivery and treatment accuracy.

Annual Operations Meeting Focuses on "Power of One"

The annual FCS Operations meeting was held in December 2014 at Raymond James Stadium in Tampa and attended by 170 practice leaders, including members from the Executive and Senior Management teams, office managers, head nurses, physician liaisons, Clinic Financial Managers and other FCS leaders. Chief Operating Officer Todd Schonherz said, "This year's theme, 'Power of One,' focused on the difference that one person can make as well as the impact one additional patient per day can have on the organization."

FCS CEO Bradley Prechtl kicked off the event with an update on the continued growth of the practice, which added 19 new physicians during 2014 and increased collections by almost 16 percent over 2013, despite the significant changes that occurred in the healthcare industry last year. Additionally, Prechtl, who serves as Chair of the FCS Foundation, also praised the remarkable growth of the non-profit, stating that it provided over $400,000 in grants for non-medical living expenses to low-income patients, an increase of 199 percent over 2013.

> "One of the meeting highlights was building bikes for kids of cancer patients."

COO Schonherz provided detail on major 2014 initiatives designed to grow adjacent business lines to support income diversification. He reported updates on Informatics, Rx-To-Go, Central Lab, Hematopathology and the Clinical Research business unit, many of which had record-setting results for 2014.

Another highlight of the 2014 meeting was the substantial progress made over the past year on the Operational Excellence Program. The Practice Operations Team developed over 200 SOP's and completed assessments at all FCS sites. According to Schonherz, the results were extremely positive and demonstrated why it really "takes a village" and a strong commitment from all FCS personnel to accomplish the mission of our organization.

Instituted in 2011, the annual Operations Meeting has grown appreciably over the past three years. In its first two years, less than 100 participants were present; 120 FCS leaders attended in 2013; and this year's 170 attendees seems to be an indication of the growing popularity of the annual event.

The meeting closed with a special team-building event that was such a hit at the 2012 Operations Meeting it returned this year by popular demand. Demonstrating the ongoing commitment Florida Cancer Specialists has to both patients and their families, meeting participants once again put their finest construction skills to work, building 24 bicycles for children of cancer patients who might not otherwise have received any gifts for the Christmas holiday.

> "Growing attendance is an indication of the increasing popularity of the annual event."

Schonherz added, "Building the bicycles and donating them to the children reminded all of us why we do what we do. It was truly a heartfelt moment and many of our management team members were in tears watching the kids and their parents receive the bikes."








ADDITIONAL SAFETY INFORMATION FOR VELCADE® (bortezomib)

WARNINGS, PRECAUTIONS, AND DRUG INTERACTIONS

- **Peripheral neuropathy:** Manage with dose modification or discontinuation. Patients with preexisting severe neuropathy should be treated with VELCADE (bortezomib) only after careful risk-benefit assessment.
- **Hypotension:** Use caution when treating patients taking antihypertensives, with a history of syncope, or with dehydration.
- **Cardiac toxicity:** Worsening of and development of cardiac failure have occurred. Closely monitor patients with existing heart disease or risk factors for heart disease.
- **Pulmonary toxicity:** Acute respiratory syndromes have occurred. Monitor closely for new or worsening symptoms.
- **Posterior reversible encephalopathy syndrome:** Consider MRI imaging for onset of visual or neurological symptoms; discontinue VELCADE if suspected.
- **Gastrointestinal toxicity:** Nausea, diarrhea, constipation, and vomiting may require use of antiemetic and antidiarrheal medications or fluid replacement.
- **Thrombocytopenia or Neutropenia:** Monitor complete blood counts regularly throughout treatment.
- **Tumor lysis syndrome:** Closely monitor patients with high tumor burden.
- **Hepatic toxicity:** Monitor hepatic enzymes during treatment.
- **Embryo-fetal risk:** Women should avoid becoming pregnant while being treated with VELCADE. Advise pregnant women of potential embryo-fetal harm.
- Closely monitor patients receiving VELCADE in combination with strong **CYP3A4** inhibitors. Avoid concomitant use of strong **CYP3A4** inducers.

ADVERSE REACTIONS

Most commonly reported adverse reactions (incidence ≥20%) in clinical studies include nausea, diarrhea, thrombocytopenia, neutropenia, peripheral neuropathy, fatigue, neuralgia, anemia, leukopenia, constipation, vomiting, lymphopenia, rash, pyrexia, and anorexia.

Please see Brief Summary for VELCADE adjacent to this advertisement and full Prescribing Information available at VELCADE-hcp.com.

Takeda ONCOLOGY

Reference: 1. Mateos M-V, Richardson PG, Schlag R, et al. Bortezomib plus melphalan and prednisone compared with melphalan and prednisone in previously untreated multiple myeloma: updated follow-up and impact of subsequent therapy in the phase III VISTA trial. *J Clin Oncol.* 2010;28(13):2259-2266.

Could you look her in the eye and tell her,

"THIS IS OUR SURVIVAL PLAN."

Plan to treat for 1 year for an overall survival (OS) advantage as demonstrated in the VISTA trial

IT'S THE MOMENT OF TRUTH. Will you tell your patients that in the VISTA trial: 1-year (50 weeks) median of VELCADE® (bortezomib) delivered a >1-year median OS advantage in combination with melphalan+prednisone (MP) vs MP alone for previously untreated multiple myeloma (median OS*: 56.4 vs 43.1 months, respectively)?[1]

VISTA TRIAL: a randomized, open-label, international, phase 3 trial (N=682) evaluating the efficacy and safety of VELCADE (bortezomib) administered intravenously in combination with MP vs MP in previously untreated multiple myeloma. After progressive disease was established, all patients were eligible to receive subsequent therapies. The primary endpoint was time to progression (TTP). Secondary endpoints were CR, ORR, PFS, and OS. At a prespecified interim analysis (median follow-up: 16.3 months), VELCADE+MP resulted in significantly superior results for TTP (median 20.7 months with VELCADE+MP vs 15.0 months with MP [p=0.000002]), PFS, OS, and ORR. Further enrollment was halted, and patients receiving MP were offered VELCADE in addition. Updated analyses were performed.

INDICATION: VELCADE (bortezomib) is indicated for the treatment of patients with multiple myeloma.

CONTRAINDICATIONS: VELCADE is contraindicated in patients with hypersensitivity (not including local reactions) to bortezomib, boron, or mannitol, including anaphylactic reactions. VELCADE is contraindicated for intrathecal administration. Fatal events have occurred with intrathecal administration of VELCADE.

*HR=0.695 (95% CI, 0.57-0.85); p<0.05.

VELCADE is on contract with Florida Cancer Specialists

VELCADE®
(bortezomib) FOR INJECTION

VELCADE®
(bortezomib) FOR INJECTION

Brief Summary

INDICATION:
VELCADE® (bortezomib) for Injection is indicated for the treatment of patients with multiple myeloma.

CONTRAINDICATIONS:
VELCADE is contraindicated in patients with hypersensitivity (not including local reactions) to bortezomib, boron, or mannitol, including anaphylactic reactions. VELCADE is contraindicated for intrathecal administration. Fatal events have occurred with intrathecal administration of VELCADE.

WARNINGS AND PRECAUTIONS:
Peripheral Neuropathy: VELCADE treatment causes a peripheral neuropathy that is predominantly sensory; however, cases of severe sensory and motor peripheral neuropathy have been reported. Patients with pre-existing symptoms (numbness, pain, or a burning feeling in the feet or hands) and/or signs of peripheral neuropathy may experience worsening peripheral neuropathy (including ≥Grade 3) during treatment with VELCADE. Patients should be monitored for symptoms of neuropathy, such as a burning sensation, hyperesthesia, hypoesthesia, paresthesia, discomfort, neuropathic pain or weakness. In the Phase 3 relapsed multiple myeloma trial comparing VELCADE subcutaneous vs intravenous, the incidence of Grade ≥2 peripheral neuropathy events was 24% for subcutaneous and 39% for intravenous. Grade ≥3 peripheral neuropathy occurred in 6% of patients in the subcutaneous treatment group, compared with 15% in the intravenous treatment group. Starting VELCADE subcutaneously may be considered for patients with pre-existing or at high risk of peripheral neuropathy.

Patients experiencing new or worsening peripheral neuropathy during VELCADE therapy may require a decrease in the dose and/or a less dose-intense schedule. In the VELCADE vs dexamethasone phase 3 relapsed multiple myeloma study, improvement in or resolution of peripheral neuropathy was reported in 48% of patients with ≥Grade 2 peripheral neuropathy following dose adjustment or interruption. Improvement in or resolution of peripheral neuropathy was reported in 73% of patients who discontinued due to Grade 2 neuropathy or who had ≥Grade 3 peripheral neuropathy in the phase 2 multiple myeloma studies. The long-term outcome of peripheral neuropathy has not been studied in mantle cell lymphoma.

Hypotension: The incidence of hypotension (postural, orthostatic, and hypotension NOS) was 8%. These events are observed throughout therapy. Caution should be used when treating patients with a history of syncope, patients receiving medications known to be associated with hypotension, and patients who are dehydrated. Management of orthostatic/postural hypotension may include adjustment of antihypertensive medications, hydration, and administration of mineralocorticoids and/or sympathomimetics.

Cardiac Toxicity: Acute development or exacerbation of congestive heart failure and new onset of decreased left ventricular ejection fraction have occurred during VELCADE therapy, including reports in patients with no risk factors for decreased left ventricular ejection fraction. Patients with risk factors for, or existing, heart disease should be closely monitored. In the relapsed multiple myeloma study of VELCADE vs dexamethasone, the incidence of any treatment-related cardiac disorder was 8% and 5% in the VELCADE and dexamethasone groups, respectively. The incidence of adverse reactions suggestive of heart failure (acute pulmonary edema, pulmonary edema, cardiac failure, congestive cardiac failure, cardiogenic shock) was ≤1% for each individual reaction in the VELCADE group. In the dexamethasone group, the incidence was ≤1% for cardiac failure and congestive cardiac failure; there were no reported reactions of acute pulmonary edema, pulmonary edema, or cardiogenic shock. There have been isolated cases of QT-interval prolongation in clinical studies; causality has not been established.

Pulmonary Toxicity: Acute Respiratory Distress Syndrome (ARDS) and acute diffuse infiltrative pulmonary disease of unknown etiology, such as pneumonitis, interstitial pneumonia, and lung infiltration have occurred in patients receiving VELCADE. Some of these events have been fatal. In a clinical trial, the first two patients given high-dose cytarabine (2 g/m^2 per day) by continuous infusion with daunorubicin and VELCADE for relapsed acute myelogenous leukemia died of ARDS early in the course of therapy. There have been reports of pulmonary hypertension associated with VELCADE administration in the absence of left heart failure or significant pulmonary disease. In the event of new or worsening cardiopulmonary symptoms, consider interrupting VELCADE until a prompt, comprehensive, diagnostic evaluation is conducted.

Posterior Reversible Encephalopathy Syndrome (PRES): Posterior Reversible Encephalopathy Syndrome (PRES; formerly termed Reversible Posterior Leukoencephalopathy Syndrome (RPLS)) has occurred in patients receiving VELCADE. PRES is a rare, reversible, neurological disorder, which can present with seizure, hypertension, headache, lethargy, confusion, blindness, and other visual and neurological disturbances. Brain imaging, preferably MRI (Magnetic Resonance Imaging), is used to confirm the diagnosis. In patients developing PRES, discontinue VELCADE. The safety of reinitiating VELCADE therapy in patients previously experiencing PRES is not known.

Gastrointestinal Toxicity: VELCADE treatment can cause nausea, diarrhea, constipation, and vomiting, sometimes requiring use of antiemetic and antidiarrheal medications. Ileus can occur. Fluid and electrolyte replacement should be administered to prevent dehydration. Interrupt VELCADE for severe symptoms.

Thrombocytopenia/Neutropenia: VELCADE is associated with thrombocytopenia and neutropenia that follow a cyclical pattern, with nadirs occurring following the last dose of each cycle and typically recovering prior to initiation of the subsequent cycle. The cyclical pattern of platelet and neutrophil decreases and recovery remain consistent in the studies of multiple myeloma with no evidence of cumulative thrombocytopenia or neutropenia in the treatment regimens studied. Monitor complete blood counts (CBC) frequently during treatment with VELCADE. Measure platelet counts prior to each dose of VELCADE. Adjust dose/schedule for thrombocytopenia. Gastrointestinal and intracerebral hemorrhage has occurred during thrombocytopenia in association with VELCADE. Support with transfusions and supportive care, according to published guidelines.

In the single-agent, relapsed multiple myeloma study of VELCADE versus dexamethasone, the mean platelet count nadir measured was approximately 40% of baseline. The incidence of bleeding (≥Grade 3) was 2% in the VELCADE arm and was <1% in the dexamethasone arm.

Tumor Lysis Syndrome: Tumor lysis syndrome has been reported with VELCADE therapy. Patients at risk of tumor lysis syndrome are those with high tumor burden prior to treatment. Monitor patients closely and take appropriate precautions.

Hepatic Toxicity: Cases of acute liver failure have been reported in patients receiving multiple concomitant medications and with serious underlying medical conditions. Other reported hepatic reactions include hepatitis, increases in liver enzymes, and hyperbilirubinemia. Interrupt VELCADE therapy to assess reversibility. There is limited re-challenge information in these patients.

Embryo-fetal Risk: Pregnancy Category D. Women of reproductive potential should avoid becoming pregnant while being treated with VELCADE. Bortezomib administered to rabbits during organogenesis at a dose approximately 0.5 times the clinical dose of 1.3 mg/m^2 based on body surface area caused post-implantation loss and a decreased number of live fetuses.

ADVERSE REACTIONS:
In the phase 3 VELCADE+melphalan and prednisone study in previously untreated multiple myeloma, the safety profile of VELCADE administered intravenously in combination with melphalan/prednisone is consistent with the known safety profiles of both VELCADE and melphalan/prednisone. The most commonly reported adverse reactions (≥10%) in this study (VELCADE+melphalan and prednisone vs melphalan and prednisone) were thrombocytopenia (48% vs 42%), neutropenia (47% vs 42%), peripheral neuropathy (46% vs 1%), nausea (39% vs 21%), diarrhea (35% vs 6%), neuralgia (34% vs <1%), anemia (32% vs 46%), leukopenia (32% vs 28%), vomiting (26% vs 12%), fatigue (25% vs 14%), lymphopenia (23% vs 15%), constipation (23% vs 4%), anorexia (19% vs 6%), asthenia (16% vs 7%), pyrexia (16% vs 6%), paresthesia (12% vs 1%), herpes zoster (11% vs 3%), rash (11% vs 2%), abdominal pain upper (10% vs 6%), and insomnia (10% vs 6%).

(Continued on next page)

Brief Summary (cont'd)

In the phase 3 study of VELCADE® (bortezomib) administered intravenously vs dexamethasone in relapsed multiple myeloma, the most commonly reported adverse reactions (>20%) were nausea (52% vs 9%), diarrhea (52% vs 11%), fatigue (39% vs 25%), peripheral neuropathies (35% vs 4%), thrombocytopenia (33% vs 3%), constipation (30% vs 8%), vomiting (29% vs 3%), and anorexia (21% vs 2%). The most commonly reported serious adverse reactions were diarrhea (3%), dehydration, herpes zoster, pyrexia, nausea, vomiting, dyspnea, and thrombocytopenia (2% each) in the VELCADE treatment group and pneumonia (4%), hyperglycemia (3%), pyrexia, and psychotic disorder (2% each) in the dexamethasone treatment group.

In the phase 3 VELCADE subcutaneous vs intravenous study in relapsed multiple myeloma, safety data were similar between the two treatment groups. The most commonly reported adverse reactions (≥10%) in this study were peripheral neuropathy NEC (37% vs 50%), thrombocytopenia (30% vs 34%), neutropenia (23% vs 27%), neuralgia (23% vs 23%), anemia (19% vs 23%), diarrhea (19% vs 28%), leukopenia (18% vs 20%), nausea (16% vs 14%), pyrexia (12% vs 8%), vomiting (9% vs 11%), asthenia (7% vs 16%), and fatigue (7% vs 15%). The incidence of serious adverse reactions was similar for the subcutaneous treatment group (20%) and the intravenous treatment group (19%). The most commonly reported SARs were pneumonia and pyrexia (2% each) in the subcutaneous treatment group and pneumonia, diarrhea, and peripheral sensory neuropathy (3% each) in the intravenous treatment group.

In a single-arm, open-label study of retreatment with intravenous VELCADE in relapsed multiple myeloma, the most common adverse drug reaction was thrombocytopenia, which occurred in 52% of patients (grade ≥3: 24%). Peripheral neuropathy was experienced by 28% of patients (grade ≥3: 6%). The incidence of serious adverse reactions was 12.3%; the most commonly reported serious adverse reactions were thrombocytopenia (3.8%), diarrhea (2.3%), and herpes zoster and pneumonia (1.5% each).

DRUG INTERACTIONS:

Bortezomib is a substrate of cytochrome P450 enzyme 3A4, 2C19 and 1A2. Co-administration of ketoconazole, a strong CYP3A4 inhibitor, increased the exposure of bortezomib by 35% in 12 patients. Monitor patients for signs of bortezomib toxicity and consider a bortezomib dose reduction if bortezomib must be given in combination with strong CYP3A4 inhibitors (eg, ketoconazole, ritonavir). Co-administration of omeprazole, a strong inhibitor of CYP2C19, had no effect on the exposure of bortezomib in 17 patients. Co-administration of rifampin, a strong CYP3A4 inducer, is expected to decrease the exposure of bortezomib by at least 45%. Because the drug interaction study (n=6) was not designed to exert the maximum effect of rifampin on bortezomib PK, decreases greater than 45% may occur. Efficacy may be reduced when VELCADE is used in combination with strong CYP3A4 inducers; therefore, concomitant use of strong CYP3A4 inducers is not recommended in patients receiving VELCADE. St. John's wort *(Hypericum perforatum)* may decrease bortezomib exposure unpredictably and should be avoided. Co-administration of dexamethasone, a weak CYP3A4 inducer, had no effect on the exposure of bortezomib in 7 patients. Co-administration of melphalan-prednisone increased the exposure of bortezomib by 17% in 21 patients. However, this increase is unlikely to be clinically relevant.

USE IN SPECIFIC POPULATIONS:

Nursing Mothers: It is not known whether bortezomib is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from VELCADE, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: The safety and effectiveness of VELCADE in children has not been established.

Geriatric Use: No overall differences in safety or effectiveness were observed between patients ≥age 65 and younger patients receiving VELCADE; but greater sensitivity of some older individuals cannot be ruled out.

Patients with Renal Impairment: The pharmacokinetics of VELCADE are not influenced by the degree of renal impairment. Therefore, dosing adjustments of VELCADE are not necessary for patients with renal insufficiency. Since dialysis may reduce VELCADE concentrations, VELCADE should be administered after the dialysis procedure. For information concerning dosing of melphalan in patients with renal impairment, see manufacturer's prescribing information.

Patients with Hepatic Impairment: The exposure of bortezomib is increased in patients with moderate and severe hepatic impairment. Starting dose should be reduced in those patients.

Patients with Diabetes: During clinical trials, hypoglycemia and hyperglycemia were reported in diabetic patients receiving oral hypoglycemics. Patients on oral antidiabetic agents receiving VELCADE treatment may require close monitoring of their blood glucose levels and adjustment of the dose of their antidiabetic medication.

OVERDOSAGE:

There is no known specific antidote for VELCADE overdosage. In humans, fatal outcomes following the administration of more than twice the recommended therapeutic dose have been reported, which were associated with the acute onset of symptomatic hypotension and thrombocytopenia. In the event of an overdosage, the patient's vital signs should be monitored and appropriate supportive care given.

PATIENT COUNSELING INFORMATION

Advise patients to contact their physicians if they experience the following symptoms:

Dehydration/Hypotension, such as dizziness, light-headedness or fainting spells, or muscle cramps.

Cardiac: swelling of feet, ankles, or legs, or other heart-related problems.

Respiratory: shortness of breath, cough, or other lung problems.

Hepatic: jaundice or right upper abdominal pain.

Dermal: rash, severe injection-site reactions, or skin pain. Discuss the option for antiviral prophylaxis for herpes virus infection.

Peripheral Neuropathy and Nervous System, such as new or worsening tingling, numbness, pain, a burning feeling in the feet or hands, or weakness in the arms or legs. Advise patients to contact their physicians if they experience symptoms possibly indicative of PRES or PML such as convulsion, persistent headache, reduced eyesight, blurred vision, confusion, lethargy, altered ability to think, or difficulty walking.

Other: increase in blood pressure, bleeding, fever, constipation, or decreased appetite.

In addition, counsel patients on the following:

Pregnancy/Nursing: Advise patients to use effective contraceptive measures to prevent pregnancy during treatment with VELCADE. Instruct them to report pregnancy to their physicians immediately. Advise patients that they should not receive VELCADE while pregnant or breast-feeding. If a patient wishes to restart breast-feeding after treatment, she should be advised to discuss the appropriate timing with her physician.

Concomitant Medications: Advise patients to speak with their physicians about any other medication they are currently taking.

Diabetic Patients: Advise patients to check their blood sugar frequently if using an oral antidiabetic medication and to notify their physicians of any changes in blood sugar level.

Ability to Drive or Operate Machinery or Impairment of Mental Ability:

Advise patients not to drive or operate machinery if they experience fatigue, dizziness, syncope, or orthostatic/postural hypotension.

Please see full Prescribing Information for VELCADE at VELCADE-hcp.com.

Takeda

ONCOLOGY

Pursuing a Culture of Excellence

'Operational Excellence' is more than just business school rhetoric at FCS

BY TISHA CREWS KELLER

When you ask the chief operations man at Florida Cancer Specialists (FCS) how he defines success, you don't necessarily get a straight answer. But the words "87 percent" come awfully close.

Eighty-seven percent is the level of customer satisfaction expectation for FCS in 2015—in a world where just 70 percent is "good" in the eyes of any MBA, and 100 percent is unattainable.

Todd Schonherz is not only the chief operating officer at FCS; he's the mind behind the company's focus on providing excellent experiences for everyone touched by the organization.

"Operational Excellence isn't perfection," Schonherz explains. "It's creating a culture of change, signified by engaged employees that are creating great experiences for our customers. It means we are looking for opportunities to do that—consistently—at all levels throughout the company."

For the COO and the rest of the executive team, Operational Excellence is the overarching strategy for the day-to-day operations of FCS. For both clinical and business staff, it means looking for opportunities to improve how we do our job at every level—from intake clerk to physician directors.

Finding ways to do better by our patients, co-workers and referring partners is what matters in this effort. And while improving efficiency is a sure-fire way to increase the company's value, it is also a great way to help every single employee get the most out of their jobs and careers.

"Keeping our attention on the patient is the basic premise," Schonherz says. "If we can keep our focus on creating a great experience for all our stakeholders, we are automatically doing the things that will help our company grow and succeed, which trickles down to every single employee."

IT'S ALL ABOUT THE PATIENTS

You can hear the pride in Schonherz's voice when he talks shop about the "net promoter score" of 83 percent that FCS earned in 2014. This business school standard measure indicates how well a company provides customer satisfaction. It's a proven way to measure customer loyalty—and the average for best in class organizations is just 70 percent.

Not one to sit on his laurels, the COO wants to increase this score to 87 percent for 2015—a goal that's certainly within reach for a motivated team.

Schonherz transitioned into the COO spot two years ago and began the Operational Excellence initiative with the full support of the board of directors and CEO.

Continuing to put emphasis on efficiency is of course a business decision, but it's also a management choice in the face of ever-increasing pressure from reimbursement challenges.

"We know that the downward pressure on reimbursement is going to become greater," Schonherz points out.

For the past two years, the COO has worked hard to make FCS a place where excellent service and staff satisfaction are cultural norms.

To help this initiative grow and succeed, Schonherz realized the effort must come from the bottom-up. That meant empowering all employees and mid-level managers to become a part of the solution for service and clinical challenges.

Special teams were formed within the FCS service silos. For instance, the Clinical Directions Team is an employee-based group that takes on responsibility for documenting best-practice-based clinical procedures. The team, made up of management-level nursing staff and others, formulates Standard Operating Procedures (SOPs) and then continually evaluates and updates them to remain current and relevant.

> "Keeping our attention on the patient is the basic premise."

Similar teams work in other areas such as research, financial counseling, pharmacy tech, laboratory and office/administrative. These teams look at the safety and efficacy of current procedures and make recommendations to the executive management team for improvement. They are responsible for helping migrate the standards throughout the staff workforce—perhaps the most important part of the excellence initiative.

"Employee engagement is the most important aspect in all of this," he says. "We want them to make suggestions and to be empowered to help formulate the solution to our never-ending challenge of balancing a great patient experience with efficiency."

In all, over 200 SOPs across all units were formulated over the past two years. They are integrated into employee performance standards and sites are annually assessed for adoption rates.

At the end of 2014, Schonherz and his staff found that, across all locations, compliance with the SOPs was 86 percent among FCS staff. For 2015, that goal is 90 percent.

To be sure, Operational Excellence is always evolving, ever-changing. For FCS, that means we can never stop striving to up our game. One of Schonherz's favorite phrases captures the challenge: We're doing it the right way today and a better way tomorrow.

"At the end of the day, no matter what type of challenges we as staff are having, our patients are going through something worse," he says. "We must create an environment of hope, respect and dignity—and ensure a great experience day in and day out."

The Clinical Side of Excellence

Since 2012, our Clinical Directions Team has developed and maintained procedures

BY TISHA CREWS KELLER

The Clinical Directions Team (CDT) at FCS is a wonderful example of the staff enabling that has grown out of the Operational Excellence pursuit.

The CDT purpose is to support the development of evidence-based, quality cancer care by developing and maintaining Standard Operating Procedures (SOPs) and ensuring that these guidelines are followed consistently by staff statewide.

The Clinical Directions Team began in 2012 with 14 members and today has grown to 21 members, including head nurses and staff working in research, pharmacy, Integrated Clinical Services, compliance, senior management and physician extenders.

And while the group began with the sole purpose of writing guidelines to help all FCS offices stay consistent, the group now has an expanded purpose and use.

Currently, the group not only drafts SOPs according to Oncology Nursing Society practice guidelines, but also serves as a sounding board and problem-solver for clinical questions and issues.

The group's officers include: Diane Cope, Ph.D., ARNP, BC, AOCNP, a nurse practitioner in the Summerlin office; Joannie Schaffer, RN, OCN, head nurse of the Sarasota downtown office; and Patty Wright, RN, BSN, OCN, head nurse and research coordinator in the Tallahassee offices.

Representatives from offices around the state and the administrative office round out the CDT and ensure input from all levels of staff. It's this mix of team members that contributes to the project success.

This team of highly skilled practitioners goes beyond just drafting and implementing SOPs. The group leads annual review and update of the SOP standards, and provides education and guidance for clinical staff implementing these procedures.

Leveraging clinical expertise with management support and buy-in from the executive staff helps the CDT streamline and fine-tune the clinical procedures at FCS. It's the wonderful melding of grassroots problem-solving and a top-down pursuit of excellence.

THE 2015 FCS CLINICAL DIRECTIONS TEAM

JENNIFER BAPTISTE
TAVARES

JEREMY BEHLING
FORT MYERS

CHRISTINA CARUSO
FORT MYERS

MELODY CHANG
FORT MYERS

DIANE COPE
FORT MYERS

DAVID CURRY
FORT MYERS

DEBORAH GUERIN
FORT MYERS

KATIE GOODMAN
SARASOTA

DONNA IRVING
FORT MYERS

SUE KEARNEY
FORT MYERS

AMANDA KIMMEL
TAMPA

DONNA OTT
WELLINGTON

MICHELLE REINHARD
LARGO

JOANNIE SCHAFFER
SARASOTA

TODD SCHONHERZ
FORT MYERS

AMY SWISHER
FORT MYERS

VERNA VALENTINE
FORT MYERS

GEORGE VALIENTE
BROOKSVILLE

KATE VELLIS
GAINESVILLE

DEBBIE VOGEL
FORT MYERS

PATTY WRIGHT
TALLAHASSEE

Up Close and Personal

Sarah Cevallos, Vice President, Revenue Cycle

BY TISHA CREWS KELLER

Sarah Cevallos is an FCS career success story. As Vice President of Revenue Cycle, she oversees all aspects of the insurance side of the business. The entire process by which FCS gets paid for clinic-based services rendered is Cevallos' responsibility. Her team focuses on everything from negotiating provider rates and services to billing insurance claims and collecting from payers.

However, her early beginnings at the company weren't so lofty.

After being laid off from a private company during the tumult of the last recession, she knew she needed career stability. She set her sights on getting her foot in the door at FCS as a Registration Coordinator in the Managed Care department. There, she learned the basics of medical benefits while verifying insurance coverage for new patients.

After applying for several positions within the company, she landed an administrative assistant position for a newly installed director, Christina Sievert. This proved to be a turning point in Cevallos' career at FCS.

"Obtaining that position is where my health care career and knowledge really took off," Cevallos says. "I was endorsed to attend meetings, and I supported projects that really stretched me."

Cevallos didn't miss an opportunity to earn her own credentials. She realized while working with Sievert that in order to continue her growth, she needed to get a more formal education in health care. She was always passionate about education and says it's the one thing she's most dedicated to in her life.

"If I could be a career student, I would enroll today," she says with a laugh. Always being open to learning is probably the most important lesson she's had over the years. Even through hard times, Cevallos realized there was something worth taking away from each situation.

After earning her master's degree with a focus in health care administration, Cevallos was now in a position to leverage her education and her hands-on knowledge at FCS. She continued to grow her career in the company, moving through various management-level positions.

"As our company grew, I was presented with a director position to oversee the Revenue Cycle team as a whole," Cevallos says.

She was promoted to Vice President in 2013, when she took on additional responsibilities to include payer credentialing and contracting.

Today, she oversees around 150 positions and more than 100 contracts. Together, she and her team manage outstanding accounts receivables and collections.

Despite her personal success and rise in the company, Cevallos counts the working relationship with her team and helping patients as the most rewarding parts of her job. Even as a young girl, she wanted to be in the service industry.

As a manager, she has found that helping others reach their maximum potential—as a staff member or even as a patient fighting a personal battle—is a rewarding side benefit of her job. Sharing her journey with others is what fulfills and enables Sarah Cevallos, and it shows.

"The secret to my success is having an impeccable support system," Cevallos maintains. "My family, friends and—of course—my team, has shaped me, pushed me and given me the remarkable amount of support needed to be successful."

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Join us as we celebrate Paris in style at a black-tie event that includes fun, fashion, delicious food and entertainment. Funds raised will support adults undergoing treatment for cancer in Florida. Each gala ticket sold, every dollar raised through sponsorships and every raffle ticket purchased counts! Be a part of a wonderful evening that will bring hope and inspiration to those who attend and to those who will benefit as a result.

Sponsored by Celgene

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Venue to be determined

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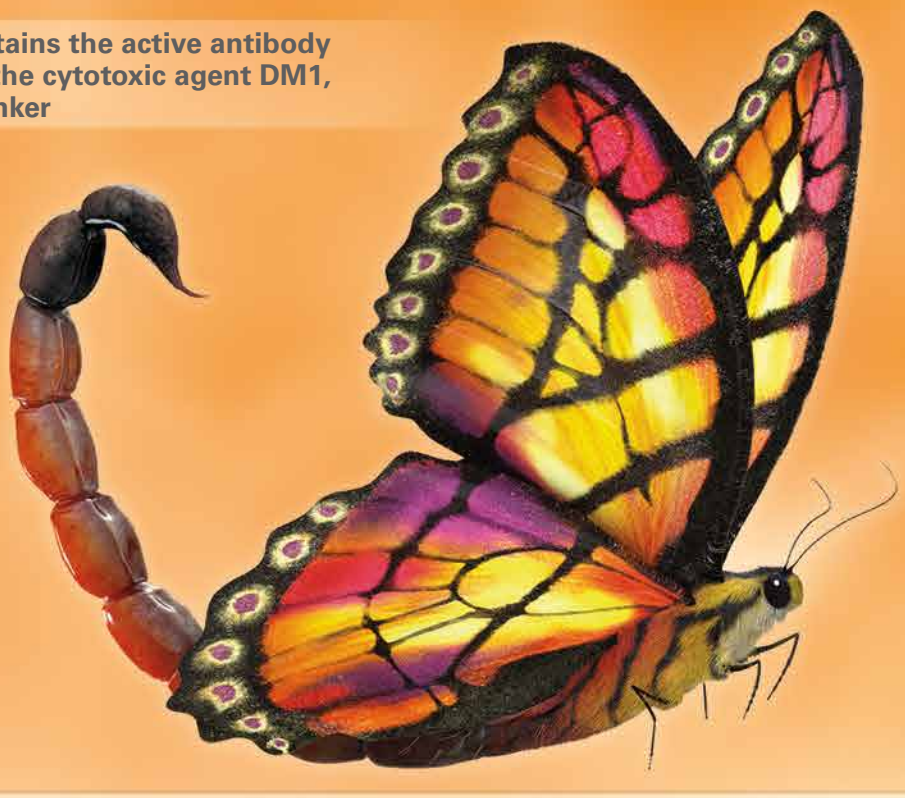
Results from the Phase III EMILIA trial KADCYLA vs lapatinib + capecitabine in patients with HER2+ metastatic breast cancer (MBC):

Proven overall survival (OS) benefit

KADCYLA contains the active antibody trastuzumab, the cytotoxic agent DM1, and a stable linker



Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: received prior therapy for metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy.

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do not substitute KADCYLA for or with trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-fetal toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the MotHER Pregnancy Registry by contacting 1-800-690-6720

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome, have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

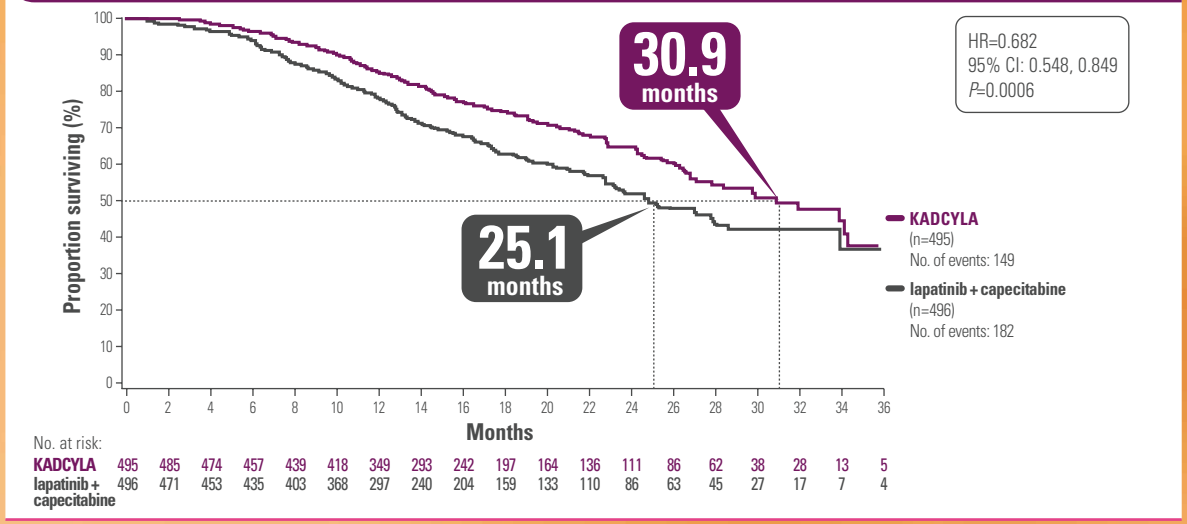
Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRRs and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRRs, especially during the first infusion

Genentech
A Member of the Roche Group

Superior efficacy with a single agent[1]

NEARLY 6-MONTH IMPROVEMENT IN MEDIAN OS[1]



Results of the randomized, open-label, Phase III EMILIA trial of KADCYLA (3.6 mg/kg IV, Day 1) vs the combination of lapatinib (1250 mg/day oral, once daily) and capecitabine (1000 mg/m^2, oral, twice daily, Days 1-14) in 21-day cycles until disease progression in HER2+ MBC patients previously treated with trastuzumab and a taxane. Primary endpoints were OS, progression-free survival (PFS), and safety.[1,2]

- 50% improvement in median PFS for KADCYLA vs lapatinib + capecitabine (9.6 months vs 6.4 months; HR=0.650; 95% CI: 0.549, 0.771; P<0.0001)[1]
- The most common adverse reactions Grades ≥3 (frequency >2%) in the KADCYLA arm were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy, and fatigue, according to NCI-CTCAE (version 3)[1]

Hemorrhage
- Hemorrhagic events, sometimes fatal, have been reported in clinical trials. In EMILIA, the incidence of ≥ Grade 3 hemorrhage was 1.8% in the KADCYLA-treated group and 0.8% in the comparator group (overall incidence 32.2% and 16.4%, respectively)
- In some of the observed cases the patients were also receiving anticoagulation therapy or antiplatelet therapy, or had thrombocytopenia; in others, there were no known additional risk factors. Use caution with these agents and consider additional monitoring when concomitant use is medically necessary

Thrombocytopenia
- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity
- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing
- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA-approved tests by laboratories with demonstrated proficiency

Extravasation
- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers
- Discontinue nursing or discontinue KADCYLA, taking into consideration the importance of the drug to the mother

Adverse Reactions
- The most common (frequency >25%) adverse drug reactions (ADR) across clinical trials with KADCYLA were nausea, fatigue, musculoskeletal pain, hemorrhage, thrombocytopenia, increased transaminases, headache, constipation, and epistaxis. In EMILIA, the most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency >2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy, and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

Please see the following pages for brief summary of full Prescribing Information, including Boxed WARNINGS.

For more information on KADCYLA, visit **KADCYLA.com**.

References: 1. KADCYLA Prescribing Information. Genentech, Inc. July 2014. **2.** Verma S, Miles D, Gianni L, et al; EMILIA Study Group. Trastuzumab emtansine for HER2-positive advanced breast cancer [published correction appears in *N Engl J Med.* 2013;368:2442]. *N Engl J Med.* 2012;367:1783-1791 and Supplementary Appendix.

Kadcyla®
ado-trastuzumab emtansine
for injection

KADCYLA® (ado-trastuzumab emtansine)

Injection for intravenous use
Initial U.S. Approval: 2013
This is a brief summary of information about KADCYLA. Before prescribing, please see full Prescribing Information.

Do Not Substitute KADCYLA for or with Trastuzumab

WARNING: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin. (2.2, 5.1)
- Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function. (2.2, 5.2)
- Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. (5.3, 8.1, 8.6)

1 INDICATIONS AND USAGE

KADCYLA®, as a single agent, is indicated for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Hepatotoxicity

Hepatotoxicity, predominantly in the form of asymptomatic, transient increases in the concentrations of serum transaminases, has been observed in clinical trials with KADCYLA *[see Adverse Reactions (6.1)]*. Serious hepatobiliary disorders, including at least two fatal cases of severe drug-induced liver injury and associated hepatic encephalopathy, have been reported in clinical trials with KADCYLA. Some of the observed cases may have been confounded by comorbidities and/or concomitant medications with known hepatotoxic potential.

Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Patients with known active hepatitis B virus or hepatitis C virus were excluded from Study 1 *[see Clinical Studies (14.1)]*. Reduce the dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases and/or total bilirubin *[see Dosage and Administration (2.2)]*. Permanently discontinue KADCYLA treatment in patients with serum transaminases > 3 x ULN and concomitant total bilirubin > 2 x ULN. KADCYLA has not been studied in patients with serum transaminases > 2.5 x ULN or bilirubin > 1.5 x ULN prior to the initiation of treatment.

In clinical trials of KADCYLA, cases of nodular regenerative hyperplasia (NRH) of the liver have been identified from liver biopsies (3 cases out of 884 treated patients, one of which was fatal). Two of these three cases of NRH were observed in the randomized trial (Study 1) *[see Adverse Reactions (6.1)]*. NRH is a rare liver condition characterized by widespread benign transformation of hepatic parenchyma into small regenerative nodules; NRH may lead to noncirrhotic portal hypertension. The diagnosis of NRH can be confirmed only by histopathology. NRH should be considered in all patients with clinical symptoms of portal hypertension and/or cirrhosis-like pattern seen on the computed tomography (CT) scan of the liver but with normal transaminases and no other manifestations of cirrhosis. Upon diagnosis of NRH, KADCYLA treatment must be permanently discontinued.

5.2 Left Ventricular Dysfunction

Patients treated with KADCYLA are at increased risk of developing left ventricular dysfunction. A decrease of LVEF to < 40% has been observed in patients treated with KADCYLA. In the randomized trial (Study 1), left ventricular dysfunction occurred in 1.8% of patients in the KADCYLA-treated group and 3.3% of patients in the lapatinib plus capecitabine-treated group *[see Adverse Reactions (6.1)]*.

Assess LVEF prior to initiation of KADCYLA and at regular intervals (e.g. every three months) during treatment to ensure the LVEF is within the institution's normal limits. Treatment with KADCYLA has not been studied in patients with LVEF < 50% prior to initiation of treatment. If, at routine monitoring, LVEF is < 40%, or is 40% to 45% with a 10% or greater absolute decrease below the pretreatment value, withhold KADCYLA and repeat LVEF assessment within approximately 3 weeks. Permanently discontinue KADCYLA if the LVEF has not improved or has declined further *[see Dosage and Administration (2.2)]*. Patients with a history of symptomatic congestive heart failure (CHF), serious cardiac arrhythmia, or history of myocardial infarction or unstable angina within 6 months were excluded from Study 1 *[see Clinical Studies (14.1)]*.

5.3 Embryo-Fetal Toxicity

KADCYLA can cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies of KADCYLA in pregnant women and no reproductive and developmental toxicology studies have been conducted with ado-trastuzumab emtansine. Nevertheless, treatment with trastuzumab, the antibody component of KADCYLA, during pregnancy in the postmarketing setting has resulted in oligohydramnios, some associated with fatal pulmonary hypoplasia, skeletal abnormalities and neonatal death. DM1, the cytotoxic component of KADCYLA, can be expected to cause embryo-fetal toxicity based on its mechanism of action.

If KADCYLA is used during pregnancy, or if the patient becomes pregnant while receiving KADCYLA, apprise the patient of the potential hazard to the fetus *[see Use in Specific Populations (8.1)]*. Verify pregnancy status prior to the initiation of KADCYLA. Advise patients of the risks of embryo-fetal death and birth defects and the need for contraception during and after treatment. Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. If KADCYLA is administered during pregnancy or if a patient becomes pregnant while receiving KADCYLA, immediately report exposure to the Genentech Adverse Event Line at 1-888-835-2555. Encourage women who may be exposed during pregnancy to enroll in the MotHER Pregnancy Registry by contacting 1-800-690-6720 *[see Patient Counseling Information (17)]*.

5.4 Pulmonary Toxicity

Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. Pneumonitis at an incidence of 0.8% (7 out of 884 treated patients) has been reported, with one case of grade 3 pneumonitis. Signs and symptoms include dyspnea, cough, fatigue, and pulmonary infiltrates. These events may or may not occur as sequelae of infusion reactions. In the randomized trial (Study 1), the overall frequency of pneumonitis was 1.2% *[see Adverse Reactions (6.1)]*.

Permanently discontinue treatment with KADCYLA in patients diagnosed with ILD or pneumonitis.

Patients with dyspnea at rest due to complications of advanced malignancy and co-morbidities may be at increased risk of pulmonary toxicity.

5.5 Infusion-Related Reactions, Hypersensitivity Reactions

Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity; treatment with KADCYLA is not recommended for these patients.

Infusion-related reactions, characterized by one or more of the following symptoms – flushing, chills, pyrexia, dyspnea, hypotension, wheezing, bronchospasm, and tachycardia have been reported in clinical trials of KADCYLA. In the randomized trial (Study 1), the overall frequency of IRRs in patients treated with KADCYLA was 1.4% *[see Adverse Reactions (6.1)]*. In most patients, these reactions resolved over the course of several hours to a day after the infusion was terminated. KADCYLA treatment should be interrupted in patients with severe IRR. KADCYLA treatment should be permanently discontinued in the event of a life-threatening IRR *[see Dosage and Administration (2.2)]*. Patients should be observed closely for IRR reactions, especially during the first infusion.

One case of a serious, allergic/anaphylactic-like reaction has been observed in clinical trials of single-agent KADCYLA. Medications to treat such reactions, as well as emergency equipment, should be available for immediate use.

5.6 Hemorrhage

Cases of hemorrhagic events, including central nervous system, respiratory, and gastrointestinal hemorrhage, have been reported in clinical trials with Kadcyla. Some of these bleeding events resulted in fatal outcomes. In the randomized trial (Study 1), the overall frequency of hemorrhage was 32.2% in the KADCYLA-treated group and 16.4% in the lapatinib plus capecitabine-treated group. The incidence of ≥ Grade 3 hemorrhage was 1.8% in the KADCYLA-treated group and 0.8% in the lapatinib plus capecitabine-treated group *[see Adverse Reactions (6.1)]*. Although, in some of the observed cases the patients were also receiving anticoagulation therapy, antiplatelet therapy, or had thrombocytopenia, in others there were no known additional risk factors. Use caution with these agents and consider additional monitoring when concomitant use is medically necessary.

5.7 Thrombocytopenia

Thrombocytopenia, or decreased platelet count, was reported in clinical trials of KADCYLA (103 of 884 treated patients with ≥ Grade 3; 283 of 884 treated patients with any Grade). The majority of these patients had Grade 1 or 2 events (< LLN to ≥ 50,000/mm^3) with the nadir occurring by day 8 and generally improving to Grade 0 or 1 (≥ 75,000/mm^3) by the next scheduled dose. In clinical trials of KADCYLA, the incidence and severity of thrombocytopenia were higher in Asian patients. Independent of race, the incidence of severe hemorrhagic events in patients treated with KADCYLA was low.

In the randomized trial (Study 1), the overall frequency of thrombocytopenia was 31.2% in the KADCYLA-treated group and 3.3% in the lapatinib plus capecitabine-treated group *[see Adverse Reactions (6.1)]*. The incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the lapatinib plus capecitabine-treated group. In Asian patients, the incidence of ≥ Grade 3 thrombocytopenia was 45.1% in the KADCYLA-treated group and 1.3% in the lapatinib plus capecitabine-treated group.

Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose *[see Dosage and Administration (2.2)]*. KADCYLA has not been studied in patients with platelet counts <100,000/mm^3 prior to initiation of treatment. In the event of decreased platelet count to Grade 3 or greater (< 50,000/mm^3) do not administer KADCYLA until platelet counts recover to Grade 1 (≥ 75,000/mm^3) *[see Dosage and Administration (2.2)]*. Patients with thrombocytopenia (< 100,000/mm^3) and patients on anti-coagulant treatment should be closely monitored during treatment with KADCYLA.

5.8 Neurotoxicity

Peripheral neuropathy, mainly as Grade 1 and predominantly sensory, was reported in clinical trials of KADCYLA (14 of 884 treated patients with ≥ Grade 3; 196 of 884 treated patients with any Grade). In the randomized trial (Study 1), the overall frequency of peripheral neuropathy was 21.2% in the KADCYLA-treated group and 13.5% in the lapatinib plus capecitabine-treated group *[see Adverse Reactions (6.1)]*. The incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the lapatinib plus capecitabine-treated group.

KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2. Patients should be clinically monitored on an ongoing basis for signs or symptoms of neurotoxicity *[see Nonclinical Toxicology (13.2)]*.

5.9 HER2 Testing

Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy because these are the only patients studied for whom benefit has been shown *[see Indications and Usage (1), Clinical Studies (14.1)]*. In the randomized study (Study 1), patients with breast cancer were required to have evidence of HER2 overexpression defined as 3+ IHC by Dako Herceptest™ or evidence of overexpression defined as FISH amplification ratio ≥ 2.0 by Dako *HER2* FISH PharmDx™ test kit. Only limited data were available for patients whose breast cancer was positive by FISH and 0 or 1+ by IHC.

Assessment of HER2 status should be performed by laboratories with demonstrated proficiency in the specific technology being utilized. Improper assay performance, including use of sub-optimally fixed tissue, failure to utilize specified reagents, deviation from specific assay instructions, and failure to include appropriate controls for assay validation, can lead to unreliable results.

5.10 Extravasation

In KADCYLA clinical studies, reactions secondary to extravasation have been observed. These reactions, observed more frequently within 24 hours of infusion, were usually mild and comprised erythema, tenderness, skin irritation, pain, or swelling at the infusion site. Specific treatment for KADCYLA extravasation is unknown. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the label:

- Hepatotoxicity *[See Warnings and Precautions (5.1)]*
- Left Ventricular Dysfunction *[See Warnings and Precautions (5.2)]*
- Embryo-Fetal Toxicity *[See Warnings and Precautions (5.3)]*
- Pulmonary Toxicity *[See Warnings and Precautions (5.4)]*
- Infusion-Related Reactions, Hypersensitivity Reactions *[See Warnings and Precautions (5.5)]*
- Thrombocytopenia *[See Warnings and Precautions (5.6)]*
- Neurotoxicity *[See Warnings and Precautions (5.7)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials, KADCYLA has been evaluated as single-agent in 884 patients with HER2-positive metastatic breast cancer. The most common (frequency ≥ 25%) adverse drug reactions (ADRs) seen in 884 patients treated with KADCYLA were fatigue, nausea, musculoskeletal pain, hemorrhage, thrombocytopenia, headache, increased transaminases, constipation and epistaxis.

The ADRs described in Table 6 were identified in patients with HER2-positive metastatic breast cancer treated in a randomized trial (Study 1) *[see Clinical Studies (14.1)]*. Patients were randomized to receive KADCYLA or lapatinib plus capecitabine. The median duration of study treatment was 7.6 months for patients in the KADCYLA-treated group and 5.5 months and 5.3 months for patients treated with lapatinib and capecitabine, respectively. Two hundred and eleven (43.1%) patients experienced ≥ Grade 3 adverse events in the KADCYLA-treated group compared with 289 (59.2%) patients in the lapatinib plus capecitabine-treated group. Dose adjustments for KADCYLA were permitted *[see Dosage and Administration (2.2)]*. Thirty-two patients (6.5%) discontinued KADCYLA due to an adverse event, compared with 41 patients (8.4%) who discontinued lapatinib, and 51 patients (10.5%) who discontinued capecitabine due to an adverse event. The most common adverse events leading to KADCYLA withdrawal were thrombocytopenia and increased transaminases. Eighty patients (16.3%) treated with KADCYLA had adverse events leading to dose reductions. The most frequent adverse events leading to dose reduction of KADCYLA (in ≥ 1% of patients) included thrombocytopenia, increased transaminases, and peripheral neuropathy. Adverse events that led to dose delays occurred in 116 (23.7%) of KADCYLA treated patients. The most frequent adverse events leading to a dose delay of KADCYLA (in ≥ 1% of patients) were neutropenia, thrombocytopenia, leukopenia, fatigue, increased transaminases and pyrexia.

Table 6 reports the ADRs that occurred in patients in the KADCYLA-treated group (n=490) of the randomized trial (Study 1). Selected laboratory abnormalities are shown in Table 7. The most common ADRs seen with KADCYLA in the randomized trial (frequency > 25%) were nausea, fatigue, musculoskeletal pain, hemorrhage, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI–CTCAE (version 3) ≥ Grade 3 ADRs (frequency >2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue.

Table 6 Summary of Adverse Drug Reactions Occurring in Patients on the KADCYLA Treatment Arm in the Randomized Trial (Study 1)

Adverse Drug Reactions (MedDRA) System Organ Class	KADCYLA (3.6 mg/kg) n=490 Frequency rate %		Lapatinib (1250 mg) + Capecitabine (2000 mg/m^2) n=488 Frequency rate %	
	All grades (%)	Grade 3 – 4 (%)	All grades (%)	Grade 3 – 4 (%)
Blood and Lymphatic System Disorders				
Neutropenia	6.7	2.0	9.0	4.3
Anemia	14.3	4.1	10.5	2.5
Thrombocytopenia	31.2	14.5	3.3	0.4
Cardiac Disorders				
Left ventricular dysfunction	1.8	0.2	3.3	0.4
Eye Disorders				
Lacrimation increased	3.3	0	2.5	0
Dry eye	3.9	0	3.1	0
Vision blurred	4.5	0	0.8	0
Conjunctivitis	3.9	0	2.3	0
Gastrointestinal Disorders				
Dyspepsia	9.2	0	11.5	0.4
Stomatitis	14.1	0.2	32.6	2.5
Dry Mouth	16.7	0	4.9	0.2
Abdominal pain	18.6	0.8	17.6	1.6
Vomiting	19.2	0.8	29.9	4.5
Diarrhea	24.1	1.6	79.7	20.7
Constipation	26.5	0.4	11.1	0
Nausea	39.8	0.8	45.1	2.5
General Disorders and Administration				
Peripheral edema	7.1	0	8.2	0.2
Chills	7.6	0	3.1	0
Pyrexia	18.6	0.2	8.4	0.4
Asthenia	17.8	0.4	17.6	1.6
Fatigue	36.3	2.5	28.3	3.5
Hepatobiliary Disorders				
Nodular regenerative hyperplasia*	0.4	ND	0	0
Portal hypertension*	0.4	0.2	0	0
Immune System Disorders				
Drug hypersensitivity	2.2	0	0.8	0
Injury, Poisoning, and Procedural				
Infusion-related reaction	1.4	0	0.2	0
Infections and Infestations				
Urinary tract infection	9.4	0.6	3.9	0
Investigations				
Blood alkaline phosphatase increased	4.7	0.4	3.7	0.4
Increased transaminases	28.8	8.0	14.3	2.5
Metabolism and Nutrition Disorders				
Hypokalemia	10.2	2.7	9.4	4.7
Musculoskeletal and Connective Tissue Disorders				
Myalgia	14.1	0.6	3.7	0
Arthralgia	19.2	0.6	8.4	0
Musculoskeletal pain	36.1	1.8	30.5	1.4
Nervous System Disorders				
Dysgeusia	8.0	0	4.1	0.2
Dizziness	10.2	0.4	10.7	0.2
Peripheral neuropathy	21.2	2.2	13.5	0.2
Headache	28.2	0.8	14.5	0.8
Psychiatric Disorders				
Insomnia	12.0	0.4	8.6	0.2
Respiratory, Thoracic, and Mediastinal Disorders				
Pneumonitis	1.2	0	0	0
Dyspnea	12.0	0.8	8.0	0.4
Cough	18.2	0.2	13.1	0.2
Epistaxis	22.5	0.2	8.4	0
Skin and Subcutaneous Tissue Disorders				
Pruritus	5.5	0.2	9.2	0
Rash	11.6	0	27.5	1.8
Vascular Disorders				
Hemorrhage	32.2	1.8	16.4	0.8
Hypertension	5.1	1.2	2.3	0.4

* Nodular Regenerative Hyperplasia and Portal Hypertension occurred in the same patient.
ND = Not determined

Table 7 Selected Laboratory Abnormalities

Parameter	KADCYLA (3.6 mg/kg)			Lapatinib (1250 mg) + Capecitabine (2000 mg/m^2)		
	All Grade %	Grade 3 %	Grade 4 %	All Grade %	Grade 3 %	Grade 4 %
Increased bilirubin	17	<1	0	57	2	0
Increased AST	98	7	<1	65	3	0
Increased ALT	82	5	<1	54	3	0
Decreased platelet count	83	14	3	21	<1	<1
Decreased hemoglobin	60	4	1	64	3	<1
Decreased neutrophils	39	3	<1	38	6	2
Decreased potassium	33	3	0	31	6	<1

Hepatic failure has been observed in two patients (0.2%) with HER2-positive metastatic breast cancer in clinical trials (n=884) with KADCYLA as single-agent.

6.2 Immunogenicity
As with all therapeutic proteins, there is the potential for an immune response to KADCYLA.

A total of 836 patients from six clinical studies were tested at multiple time points for anti-therapeutic antibody (ATA) responses to KADCYLA. Following KADCYLA dosing, 5.3% (44/836) of patients tested positive for anti-KADCYLA antibodies at one or more post-dose time points. The presence of KADCYLA in patient serum at the time of ATA sampling may interfere with the ability of this assay to detect anti-KADCYLA antibodies. As a result, data may not accurately reflect the true incidence of anti-KADCYLA antibody development. In addition, neutralizing activity of anti-KADCYLA antibodies has not been assessed.

Immunogenicity data are highly dependent on the sensitivity and specificity of the test methods used. Additionally, the observed incidence of a positive result in a test method may be influenced by several factors, including sample handling, timing of sample collection, drug interference, concomitant medication and the underlying disease. Therefore, comparison of the incidence of antibodies to KADCYLA with the incidence of antibodies to other products may be misleading. Clinical significance of anti-KADCYLA antibodies is not yet known.

7 DRUG INTERACTIONS

No formal drug-drug interaction studies with KADCYLA have been conducted. *In vitro* studies indicate that DM1, the cytotoxic component of KADCYLA, is metabolized mainly by CYP3A4 and to a lesser extent by CYP3A5. Concomitant use of strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, and voriconazole) with KADCYLA should be avoided due to the potential for an increase in DM1 exposure and toxicity. Consider an alternate medication with no or minimal potential to inhibit CYP3A4. If concomitant use of strong CYP3A4 inhibitors is unavoidable, consider delaying KADCYLA treatment until the strong CYP3A4 inhibitors have cleared from the circulation (approximately 3 elimination half-lives of the inhibitors) when possible. If a strong CYP3A4 inhibitor is coadministered and KADCYLA treatment cannot be delayed, patients should be closely monitored for adverse reactions.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Pregnancy Category D *[see Warnings and Precautions (5.3)]*

Risk Summary

KADCYLA can cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies of KADCYLA in pregnant women. No reproductive and developmental toxicology studies have been conducted with ado-trastuzumab emtansine. Nevertheless, two components of KADCYLA (trastuzumab and DM1) are known or suspected to cause fetal harm or death when administered to a pregnant woman. If KADCYLA is administered during pregnancy, or if a patient becomes pregnant while receiving KADCYLA, apprise the patient of the potential hazard to the fetus. Patients should be advised to use effective contraception during treatment with KADCYLA and for 6 months following the last dose of KADCYLA.

If KADCYLA is administered during pregnancy or if a patient becomes pregnant while receiving KADCYLA, immediately report exposure to the Genentech Adverse Event Line at 1-888-835-2555. Encourage women who may be exposed during pregnancy to enroll in the MotHER Pregnancy Registry by contacting 1-800-690-6720 *[see Patient Counseling Information (17)]*.

Human Data

In the post-marketing setting, treatment with trastuzumab during pregnancy has resulted in cases of oligohydramnios, some associated with fatal pulmonary hypoplasia, skeletal abnormalities and neonatal death. These case reports described oligohydramnios in pregnant women who received trastuzumab either alone or in combination with chemotherapy. In some case reports, amniotic fluid index increased after trastuzumab was stopped. In one case, trastuzumab therapy resumed after the amniotic fluid index improved, and oligohydramnios recurred.

Animal Data

There were no reproductive and developmental toxicology studies conducted with ado-trastuzumab emtansine. DM1, the cytotoxic component of KADCYLA, disrupts microtubule function. DM1 is toxic to rapidly dividing cells in animals and is genotoxic, suggesting it has the potential to cause embryotoxicity and teratogenicity. In studies where trastuzumab was administered to pregnant monkeys at doses up to 25 mg/kg (about 7 times the clinical dose), trastuzumab crossed the placental barrier during the early and late phases of gestation. The resulting concentrations of trastuzumab in fetal blood and amniotic fluid were approximately 33% and 25%, respectively, of those present in the maternal serum but were not associated with adverse findings.

8.3 Nursing Mothers
It is not known whether KADCYLA, specifically, is excreted in human milk, but IgG is known to be excreted in human milk. In lactating monkeys, trastuzumab was excreted in small amounts (about 0.3% of maternal serum concentrations) in breast milk after post-partum doses of 25 mg/kg (about 7 times the clinical dose of KADCYLA). Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from KADCYLA, a decision should be made whether to discontinue nursing or discontinue KADCYLA, taking into account the importance of the drug to the mother *[see Warnings and Precautions (5.3)]*.

8.4 Pediatric Use
Safety and effectiveness of KADCYLA have not been established in pediatric patients.

8.5 Geriatric Use
Of 495 patients who were randomized to KADCYLA in the randomized trial (Study 1) *[see Clinical Studies (14.1)]*, 65 patients (13%) were ≥ 65 years of age and 11 patients (2%) were ≥ 75 years of age. In patients ≥ 65 years old (n=138 across both treatment arms) the hazard ratios for progression-free survival (PFS) and Overall Survival (OS) were 1.06 (95% CI: 0.68, 1.66) and 1.05 (95% CI: 0.58, 1.91), respectively.

Population pharmacokinetic analysis indicates that age does not have a clinically meaningful effect on the pharmacokinetics of ado-trastuzumab emtansine *[see Clinical Pharmacology (12.3)]*.

8.6 Females of Reproductive Potential
KADCYLA can cause embryo-fetal harm when administered during pregnancy. Counsel patients regarding pregnancy prevention and planning. Advise females of reproductive potential to use effective contraception while receiving KADCYLA and for 6 months following the last dose of KADCYLA.

If KADCYLA is administered during pregnancy or if the patient becomes pregnant while receiving KADCYLA, immediately report exposure to the Genentech Adverse Event Line at 1-888-835-2555. Encourage women who may be exposed during pregnancy to enroll in the MotHER Pregnancy Registry by contacting 1-800-690-6720 *[see Patient Counseling Information (17)]*.

8.7 Renal Impairment
No dedicated renal impairment trial for KADCYLA has been conducted. Based on the population pharmacokinetics, as well as analysis of Grade 3 or greater adverse drug reactions and dose modifications, dose adjustments of KADCYLA are not needed in patients with mild (creatinine clearance [CLcr] 60 to 89 mL/min) or moderate (CLcr 30 to 59 mL/min) renal impairment. No dose adjustment can be recommended for patients with severe renal impairment (CLcr less than 30 mL/min) because of the limited data available *[see Clinical Pharmacology (12.3)]*.

8.8 Hepatic Impairment
In vitro studies in human liver microsomes indicates that DM1 is metabolized by CYP3A4/5. The influence of hepatic impairment on the pharmacokinetics of ado-trastuzumab emtansine conjugate has not been determined.

10 OVERDOSAGE

There is no known antidote for overdose of KADCYLA. In clinical trials, overdose of KADCYLA has been reported at approximately two times the recommended dose which resulted in Grade 2 thrombocytopenia (resolved 4 days later) and one death. In the fatal case, the patient incorrectly received KADCYLA at 6 mg/kg and died approximately 3 weeks following the overdose; a cause of death and a causal relationship to KADCYLA were not established.

17 PATIENT COUNSELING INFORMATION

- Inform patients of the possibility of severe liver injury and advise patients to immediately seek medical attention if they experience symptoms of acute hepatitis such as nausea, vomiting, abdominal pain (especially RUQ abdominal pain), jaundice, dark urine, generalized pruritus, anorexia, etc. *[see Warnings and Precautions (5.1)]*.
- Advise patients to contact a health care professional immediately for any of the following: new onset or worsening shortness of breath, cough, swelling of the ankles/legs, palpitations, weight gain of more than 5 pounds in 24 hours, dizziness or loss of consciousness *[see Warnings and Precautions (5.2)]*.
- Advise pregnant women and females of reproductive potential that KADCYLA exposure can result in fetal harm, including embryo-fetal death or birth defects *[see Warnings and Precautions (5.3), Use in Specific Populations (8.1, 8.6)]*.
- Advise females of reproductive potential to use effective contraception while receiving KADCYLA and for 6 months following the last dose of KADCYLA *[See Warnings and Precautions (5.3) and Use in Specific Populations (8.1, 8.6)]*.
- Advise nursing mothers treated with KADCYLA to discontinue nursing or discontinue KADCYLA, taking into account the importance of the drug to the mother *[see Use in Specific Populations (8.3)]*.
- Encourage women who are exposed to KADCYLA during pregnancy to enroll in the MotHER Pregnancy Registry by contacting 1-800-690-6720 *[see Warnings and Precautions (5.3) and Use in Specific Populations (8.1, 8.6)]*.

KADCYLA® (ado-trastuzumab emtansine)

Genentech
A Member of the Roche Group

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FCS Profile – Dr. Lowell Hart

After 26 Years, Dr. Lowell Hart is Still 'All In'

BY ZANDRA WOLFGRAM

Dr. Lowell Hart is just that—all heart. At 67, he is just as passionate about his patients, practicing medicine, the role of research and the future of the field as he was when he first scrubbed in to a summer college job in the OR at Columbia Presbyterian Medical Center in his hometown of New York City.

Hart marvels now at how he and his Columbia University roommate were passing instruments in the operating room after just two weeks of training.

"You don't see that anymore," he says with a laugh.

It was the 1970s, and Hart had just completed his freshman year as a political science major, but as soon as he stepped into the OR, he experienced what he calls a "magic" moment.

"I really loved it. I thought, 'This is for me. I'm all in. That's it … I'm going pre-med,'" he recalls.

Hart graduated from medical school at State University of New York at Syracuse in 1980, but after it snowed 180 inches his senior year, he and some classmates "got the bright idea to head south." He relocated to the Sunshine State to complete his internship and residency at the University of Miami.

There he met William Harwin, who while already a physician went on to become an oncologist, founder and president of Florida Cancer Specialists & Research Institute. The two Long Islanders shared an interest in hematology and a deep respect for research. Hart eventually left to do a fellowship at Duke University, where he focused mainly on breast cancer research, his "first academic love."

The classmates kept in touch over the years. After Hart's fellowship, he stayed on and joined the faculty at Duke. Though Hart confesses he had a lot of prestige, he wasn't earning much. With wife Cynthia expecting baby number three, he was moonlighting in emergency rooms and urgent care centers to make ends meet. One day in 1988, Harwin called to follow up on a patient at Duke, and when the person who answered the phone informed Harwin that Hart wasn't all that happy, he had him paged and offered him a job on the spot. Hart recalls, "He invited me to come work with him in Florida and made me an offer I couldn't refuse, as they say."

On Jan. 1, 1989, Hart became one of the "originals"—a handful of physicians handpicked by Harwin in the mid- to late 1980s to lead and shape what is now Florida Cancer Specialists & Research Institute. Today, Hart is the scientific director of clinical research and director of the FCS Drug Development Program.

Over his 26-year tenure, Hart has helped to elevate FCS to one of the leading oncology/hematology private practices in the country. While establishing a thriving private practice in Fort Myers, he was seminal in developing successful long-term partnerships with some of the leading research centers in the nation, such as the Sarah Cannon Research Network (SCRI). His affiliation with SCRI led to establishing the Early Phase Clinical Trial research program, which remains one of only a few in the nation led by a private practice.

Hart's research-based experience was seminal in helping to establish the Multidisciplinary Breast Clinic at Lee Memorial Health System in Fort Myers. Designed as a integrated

approach to breast cancer, radiation oncologists, surgeons and medical oncologists meet concurrently and then gather with pathologists and radiologists to review films and discuss the patient's care as a team.

"We are proud to have this here. It's just like they do it at Duke, Moffitt and Harvard, and we have it right here in Fort Myers," he says.

Hart has trained physicians who are now leading experts across the nation at Harvard, Duke and the like. He is well published and is frequently invited to medical meetings and conferences as a guest speaker. When we caught up with Hart for this story, he had just given a talk to doctors at Wake Forest University in Winston-Salem, North Carolina, about something he has seen a lot of—change.

"I talked about the future of cancer drug development," he says. "I talked about how things have moved from fairly toxic treatments to more and more targeted agents and the precision (that) medicine is having in this new era, and what FCS is doing to move things along."

Though no one questions that getting more drugs approved faster is the goal, getting there is no small task or cost.

"The majority of new drugs can be a decade or more of development time, and many of those fail," Hart says. "The cost spent in development for a drug to go from test tube to FDA approval is a billion dollars. When it comes to research, time is money, so we need to find ways to speed things up."

One thing racing along is FCS' efforts. Hart encourages FCS' research teams to leverage their partnerships and affiliations to find even more innovative ways of doing trials and hitting targets, such as refining molecular testing.

The more challenging the problem, the more complicated the disease, and the more Hart's interest is piqued.

"I don't like dealing with any bologna. If a patient is coming in because their white blood count went up one point, I'm the first one to try to pawn that off… Give me real illness," he jokes.

It's easy to see how Hart's approachability and sense of humor put his patients at ease. It's mutual. After nearly three decades, it's his patients that keep him inspired.

"It sounds funny to say, but there are doctors that don't like taking care of sick people," he says. "Then there are those who want a stethoscope on and help pull their patients back from the hole, and I guess I'm one of those. These patients are courageous. They are in the fight of their life. How could you not want to use all of your skills and all you've learned to help them?"

The deep reward that comes from helping to extend and save lives is why oncology called to Hart. And although he feels a sense of pride and accomplishment when he considers that a good majority of the drugs "changing the face of cancer treatment in the past decade" are the result of the hard work and dedication of the research division he started, he's not quite ready to rest on his laurels.

For Hart, whether he's talking about his growing family of six children and three grandchildren or the next medical breakthrough on the horizon, he's sure the best is yet to come—and he can't wait to play a part.

"I am glad I'm in my mid-60s and am still going strong. If I retired now, I would miss all the fun stuff," he says.

Beth Wittmer

BY WENDY O. DIXON

Florida Cancer Specialists & Research Institute's Beth Wittmer knew from a young age she had a knack for nursing. Though she hesitates to seem boastful when describing herself as nurturing and caring, she distinctly recalls a tendency toward serving the sick.

"Since I was a little girl I wanted to be a nurse. I naturally have that personality of wanting to take care of the sick, so I think it was meant to be," she says. "I knew I wanted that hands-on approach with people."

Growing up in northern Alberta, Canada, Wittmer had a relatively large nuclear family, with three brothers and three sisters, but no extended family nearby.

"We lived in a small town, which I liked," she says. "And since we grew up away from extended family, we had friends who became family. We grew up with a lot of snow, and I loved skiing—it's my favorite sport—but don't like living in it, so I go visit about once a year."

While all her siblings remained there, Wittmer and her husband, whom she met in Kansas while attending nursing school, moved to Indiana, where she later graduated with her nursing degree from Vincennes University. Having lived in the Sunshine State for the past 23 years, her family is happy to come south to enjoy the warmth of Florida.

As head nurse/office manager at Lakewood Ranch, one of the 80 sites under Florida Cancer Specialists (FCS), Wittmer also is direct supervisor of the facility, which has five nurses, one pharmaceutical technician, two medical assistants and two front-office staffers.

"I switched to oncology over nine years ago to get out of the hospital setting," she says, recalling spending 15

years in the hospital setting working cardiac, emergency and intensive care. "Oncology was the one area I was sure I wouldn't work in because years ago the treatment options were limited and the hospital setting was strictly dying patients. Now that's changed. It's turned out to be an absolute blessing for me to work with cancer patients as they have taught me to be grateful and count my blessings in my own life."

Her day begins overseeing the flow and management of the entire office. Some days that means jumping in to fill in as a nurse in the infusion room, help in the lab, assist rooming patients or answer phone calls and assist in scheduling patients.

"We have nearly 100 people going through the office, some getting infusions or getting shots related to chemo," she says. "If our day is busy, I'm out trying to assist in whatever area is needed, otherwise I am working in my office to stay on top of the administrative role." The office treats a wide variety of cancers, including prostate, breast, lung, lymphomas, melanoma, ovarian and kidney.

Wittmer says she and her staff see their patients as extended family while caring for them frequently and seeing them often.

"I have become quite close to many patients and their families," she says. "Being a nurse for many years has taught me that death is a part of life, and I am able to separate myself from becoming too emotionally involved. I get the privilege of walking alongside the patient and their family and cheer them on in their journey."

While caring for their patients is their utmost priority, the staff at Lakewood Ranch know how to have fun in the office, too.

"We have Jean Fridays for the staff, and we pay a dollar to wear jeans that day," Wittmer explains. "The money is put into a fund that we use to buy gifts cards at Publix and give them to patients in need. We also have a food pantry that we purchase BOGO (buy one, get one free) items for and we give out to those in need as well."

Wittmer says she's thrilled to go to work each day, working alongside a stellar group of professionals.

"I'm really blessed to work with great people," she adds. "We have such a great team. I wouldn't be in this position without their support of me in this role."

Balancing her career and personal life is tilted toward her four children, with a daughter and son in high school and one daughter in college, as well as one daughter who just got married.

"I attend a lot of ballgames," she says. "My college-aged daughter plays on the volleyball team, so we travel to games in the mid-state, and two of the high school children are active in sports as well. At this point in my life it revolves around them. But in my spare time I enjoy reading and exercise."

It looks as though the young girl who wanted to be a nurse was right, Wittmer says. She has the perfect job for her and feels great satisfaction every day.

"There are times when I thought about switching to something else," she says. "Then I remember the rewards of caring for people, and I don't think I'd be suited for anything else."

"We have such a great team. I wouldn't be in this position without their support of me in this role."

Orlando Downtown puts patient comfort and well-being above all else

BY WENDY O. DIXON

In the heart of Orlando, on Orange Avenue, the Orlando Downtown office of Florida Cancer Specialists & Research Institute (FCS) is centrally surrounded by all local hospitals, making it convenient for patients who need to transfer to the recently renovated location.

FCS, the largest independent medical oncology and hematology practice in the U.S., has more than 170 physicians, 110 nurse practitioners and physician assistants in its 80 locations.

The top-quality team of 23 staffers at the Orlando Downtown office works to improve quality of life during treatment and establish strong doctor-patient relationships, offering the latest in technology and medical care, and is committed to providing world-class cancer care in a community-based setting.

Led by Drs. Geetha Akula and Maria Regina Flores, who founded the practice, as well as Meera Iyengar, the Orlando Downtown office sees around 80 to 90 patients per day and treats a wide variety of cancers. The recent renovation, which included an expanded waiting room, larger lab and draw area, helps with patient comfort during their stay while getting treatment.

"The larger area makes it easier for the patients," says Office Manager Maria Langhorst, who joined the practice in 2010. "The patients can now wait much more comfortably before they are called in for treatment. And the larger space helps with flow." The creamy colors of the newly painted walls are made up of calming neutrals.

The renovation was done with the patients' comfort in mind.

"We try to make the patients feel like this is their second home; we try to make it as comfortable as possible," Langhorst says. "They're not just a patient here, they're almost like family."

Recognized by the American Society of Clinical Oncology with a national Clinical Trials Participation Award, FCS offers patients access to more clinical trials than any private oncology practice in Florida. In addition to the clinical trials, patient care has vastly improved, thanks to technology and medical advances that make it more convenient for the patients.

"Even seven or eight years ago, we were not able to give pills to patients. They had to come into the office and sit for hours at a time, spending most of their days here," Dr. Akula says. "Now patients can take their pills at home; the quality of life is much better. Patient-doctor relationship is the most important thing in medicine. You develop a bond with the patient and their families, especially in the field of oncology. That means a lot to the patients, as well as to us. It helps us understand what they're going through so we can help them better."

Dr. Flores, an oncologist for 17 years, recalls that during the early days of her training, her mentor told her the job is about knowing three things— how to treat, how to care and how to communicate.

"I think it's an exciting field. There's a lot of research in it; it will always be changing," she says. "In that sense, it always makes you excited, giving you something to look forward to, and there's always that chase for the cure."

In addition to their board certifications in medical oncology, internal medicine and hematology, Akula and Flores each speak four languages—English, Spanish, Kapampangan, Tagolog, Telugo, Hindi and Tamil, which helps in communicating with patients in multicultural Central Florida. Dr. Iyengar has held various research positions, and her work has been published in such prestigious journals as the International Journal of Radiation Oncology, Biology, Physics, the Journal of Surgical Research and the Journal of Pediatric Surgery.

Whether a patient spends five minutes or up to nine hours at the Orlando Downtown office, and whether they are receiving their treatments daily or weekly, patients know the staff, and the staff knows each patient, Langhorst says. The new reclining chairs and warm blankets, as well as an additional spot for one family member, help keep patients as comfortable as possible during a visit.

Louia C. Atkins, who has been getting treatment for lung cancer and an enlarged lymph node, attests to the commitment to quality of care the staff provides to its patients.

"Everyone on staff is kind, courteous and helpful," he says. "They make sure to stick with the appointment so I can get in and get out." Atkins spends anywhere from two to seven hours getting treatment. "Patients can watch TV, read or play those electronic games. But I'm old school," he laughs. "So I bring my CD player and headphones and listen to soul, gospel music and jazz. People seem to get a kick out of seeing me bob my head to the beat.

"The staff will do all they can to accommodate patients' needs, and try to make it as convenient as possible," Atkins says, raving in particular about Marc Peiper, the nurse practitioner for Akula. "He calls in prescriptions for me, he's friendly and always greets you with a smile. But the best thing is that they discovered the lymph node early on; I didn't even feel it, so I'm grateful they caught it early. I thank God for them."

FCS' Early-Phase Clinical Trials

Bringing more patients new and better drug therapies sooner than ever before

BY ZANDRA WOLFGRAM

You could say Dr. Manish Patel has always liked the "fast lane." Whether on or off the clock, he is most comfortable when he is moving forward. He even talks fast, although the Florida Cancer Specialists & Research Institute (FCS) physician is certainly not all talk.

In just four years, Patel and his dedicated staff of more than a dozen have grown FCS' Sarasota Drug Development Unit to the point where it now has a menu of more than 40 active early-phase clinical trials. He and his team enrolled more than 160 patients last year. And with the scheduled addition of a second physician this summer, the program is slated to grow even more.

The scope of FCS' Early Phase Clinical Trials research program is comparable to those found in prestigious academic cancer centers around the country. In fact, 10 percent of the patient referrals are made by academic centers and practices outside of FCS. And the industry has duly taken note by citing many of FCS' patient trials in abstracts presented at important national and international medical conferences, which has given the program even more exposure and prestige.

Patel is proud of the program and points out that "one could argue the quality of our program at FCS is even better than those at academic centers." But he is quick to share the credit for the success of the program.

"This would not have been possible without our research staff, William Harwin, Lowell Hart, Katie Goodman, the SCRI (Sarah Cannon Research Institute), all of the participating FCS physicians and our excellent administration," he says.

Though there is still work to do, Patel is pleased with the progress that has been made in a relatively short span of time.

"When I look back, it's rewarding to see where we started. We began with just myself and a staff of two, and now we have a hardworking, knowledgeable team of more than 12 and are still growing," he says.

What initially attracted Patel to FCS is what continues to keep the high-energy physician engaged—the company's visionary leadership.

"It's an unbelievable organization full of passionate people who are interested in going to the next level. It's tightly run, detail-oriented, and that is a fit for my personality," he says.

It's a demanding, fast-paced, detail-oriented, sub-specialized position that draws on all of Patel's training. Being curious, hardworking and motivated, he wouldn't want it any other way. This is exactly what he sought when he entered the field of medicine and precisely why he chose oncology.

"I wanted something that was challenging. Oncology was one of the fastest-growing fields, and that attracted me. I could sense it was changing in a very positive direction, and I wanted to be a part of that," he says.

A native son of Florida, Patel was born in Daytona Beach and grew up in Dunedin—just north of Clearwater on the Suncoast. He received his undergraduate degree at the University of Florida, his graduate degree from University of Miami, and was a fellow at H. Lee Moffitt Cancer Center & Research Institute in Tampa. He did leave Florida to complete his residency in Nashville, Tennessee, at Vanderbilt University Medical Center.

Today, Patel lives and works in Sarasota—just an hour south of where he was raised—with his wife, Nidhi, and their 5-year-old son, Ishan, and infant daughter, Leena. When he's not spending time with this young family, Patel enjoys all kinds of sports and nearly anything action-packed that brings him outdoors.

Patel isn't the only thing moving fast these days. The trend of targeted therapies is swiftly transforming nearly all aspects of clinical trials. Larger trials mean more patients can be treated and, therefore, a greater number of drugs are being approved in less time than ever before. More options for patients allows FCS to offer even better care.

"It's so nice to be able to offer these therapy options to our patients earlier and with much less toxicity than what we have seen in the past," Patel says.

One of the things that attracted Patel to oncology was that it was a rapidly evolving field. The recent advancements in early-phase clinical trials are a clear illustration, and Patel is eager for all of his FCS colleagues to be made well aware.

"One of the things we at FCS need to understand is that trials are a lot different now," he explains. "Decades ago, early-phase clinical trials were for patients who received many prior lines of chemotherapy. Now these trials are focusing on targeted populations who have received minimal therapy; some are restricted to just one or two lines. So a lot has changed over the past decade, even the last five years."

As with any test, final results are ultimately key.

"The criteria are stricter, and we are no longer working with small trials where all that we focused on was dose and toxicity," Patel says. "Now efficacy is playing a large role in deciding whether to move forward with the drug."

Patel can name success stories one after the other that came from early-phase clinical trials. Merck's Pembrolizumab is just one of many examples of a targeted therapy drug approved in September off of a Phase I trial. It has shown to be an effective IV PD-1 inhibitor to be used for metastatic melanoma.

Is the breakneck speed to market cause for concern? Patel says it's too early to know what the latent side effects may be down the road, but he remains resolute in the value that clinical trials bring to advancing cancer care forward.

"Because the early-phase clinical trials are so much larger, more precisely done, and highly targeted, the benefits outweigh the risks of getting accelerated approval from these drugs," he says.

For Breast Cancer in Older Women, Skip the XRT

At San Antonio Breast, the PRIME II study was presented that asked the question: Can women aged 65 years and older, after lumpectomy for an ER positive, lymph node negative breast cancer (3cm or less), just skip radiation altogether and only be treated with good surgery and arimidex? The answer is yes, for the English authors anyway, and they say that this has already changed practice in the United Kingdom. You'll have to look at the details and decide if the answer is yes for your individual patients.

FINALLY, A GOOD STRATEGY FOR SMALL HER 2 POSITIVE TUMORS

We scratch our heads and twist ourselves in knots over those women with small, lymph node negative but HER 2 Positive tumors. We "feel" they need chemo along with their Herceptin but very few studies have included any women with tumors less than one or two centimeters. Do you sentence them to Adriamycin and all of its potential long-term side effects? Eric Winer and his team knew that a placebo trial in HER 2 positive disease was out of the question so they designed and conducted, and then presented, the APT trial of weekly Taxol times 12 with one year of Herceptin in node-negative, HER 2 positive women with tumors three centimeters or less. They did great, with 99 percent disease-free at three years and very little toxicity. This is now considered a very reasonable adjuvant option in these women.

CONFUSED ABOUT LYNCH SYNDROME TESTING?

Join the club. This is an important "new" wave in cancer and very few of us have a mastery of the full algorithm for testing, which can include both phenotype and genotype tumor testing in addition to germline genetic testing of the patient. Dr Doug Hartman at the University of Pittsburgh says it is actually pretty easy—everyone with stage IV colon cancer should have their tumor tested by the most sensitive method: MSI polymerase chain reaction (MSI-PCR) along with DNA mismatch repair protein IHC. At Pitt they adopted "Universal Screening" this year based on their large prospective study (Journal Of Human Pathology, Sept 2013). Age, tumor location, microsatellite instability testing are just not good enough—you'll miss one-in-five Lynch patients, and that's too many.

GBM RESPONDS TO VALCYTE

GBM is awful. Glaciers move faster than GBM scientists. But in a letter to the New England Journal, the Swedes stirred up a hornet's nest by concluding that in their 42 cases of GBM the anti-CMV drug Valcyte, when given for six months, increased the life expectancy of these folks from only one year to two years. That qualifies as "awesome" in this tragic disease. In 250 cases they examined before the study, they found only one patient who was CMV negative. So this may join Kaposi's Sarcoma and cervical cancer as neoplasms caused by an infectious disease.

SO SHE IS JAK 2 NEGATIVE? MAYBE WE CAN EXPLAIN...

The patient with obvious myeloproliferative disorder but negative JAK 2 testing is a puzzle. But the geniuses in Cambridge, England, think they can explain this in the majority of patients. They found that 84 percent of these folks had a somatic mutation in the CALR gene. Soon, we will include this testing when we don't see a JAK 2 mutation. (NEJM, Dec. 19, 2013)

BUMP FISTS, DON'T SHAKE HANDS

I live with a germaphobe so this caught my eye. Researchers from the West Virginia School of Medicine did a cute experiment. They had docs go through the hospital and first, shake hands, and then, fist bump. Shaking hands resulted in tons more nasty germs (common sense). But, get this, even after washing, the handshakes resulted in 84 percent higher colony counts. Fist bump your friends in the hospital. Your family will thank you.

COKE? PEPSI? ENDOMETRIAL CANCER?

A huge study of 20,000 women conducted at the University of Minnesota showed, pretty convincingly, that higher consumption of sugary drinks (like Coke, Pepsi, Hawaiian Punch, Lemonade, Seven-UP) resulted in a 78 percent increase in endometrial cancer in post-menopausal women. The slope of the curve is near one. The more you drink, the higher your risk.

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