FCS THE MAGAZINE

FALL 2020

COVID-19:
Responding to the new normal

SARAH CANNON Research Institute | FLORIDA CANCER SPECIALISTS & Research Institute | ION Solutions AmerisourceBergen

NATHAN H. WALCKER, CHIEF EXECUTIVE OFFICER:

Since joining the organization as CFO just over one year ago, I have been immersed with our Executive Board, physicians and nearly 4,000 team members in the unwavering pursuit of excellence in delivering world-class patient care and the collective desire to advance community-based oncology.

Like most of us, I never imagined that our lives would be upended by a global pandemic.

Despite the many challenges of the COVID-19 crisis, our FCS clinical locations have remained open and fully committed to treating our patients safely and responsibly, with minimal disruption. Our team took swift action, adapted operations and enacted stringent procedures and safeguards to address our three highest priorities – keeping patients safe, keeping physicians and employees safe, and providing uninterrupted care and service.

In these pages, we spotlight some of the remarkable individuals and teams whose efforts and innovation have protected our patients and each other so that we can continue providing critical treatment. While there is much we still don't know about COVID-19 and its future course, FCS will build upon our strong foundation and successfully navigate the dynamic opportunities ahead.

Thank you for your ongoing support of our efforts.

LUCIO GORDAN, MD, PRESIDENT & MANAGING PHYSICIAN:

Telehealth has become an important aspect of providing care to our patients during the COVID-19 pandemic.

Florida Cancer Specialists was among the first practices in Florida to launch telehealth services and resources for cancer patients. Through the use of secure video chat, FCS physicians, advanced practice providers and other clinicians consult with patients remotely, share laboratory results, treatment plans and collaborate with other health team members.

FCS Chief information Officer Mark Moch and his team were able to successfully integrate multiple electronic platforms, in a very compressed period of time, to ensure the critical access needed for continuum of care and communication. In this issue, you can read more about telehealth and how patients and physicians have responded to this technology.

And don't miss the "Clinical Research Update" with FCS Director of Research Operations Dr. James Reeves, Jr., who discusses how clinical trials, through our strategic partnership with Sarah Cannon Research Institute, continue to drive advances in oncology treatment.

We expect 2020 to continue presenting challenges for community oncology; however, FCS is in a strong leadership position to meet every test and always put our patients first. We continue to succeed because of the dedication and excellence of our physicians, nurses and FCS staff members. Thank you for all that you do!

FCS THE MAGAZINE

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We welcome your feedback, article suggestions and photos (high resolution please).

Email to FCSCommunications@FLCancer.com

Responding to a Pandemic

FCS prioritized patient and employee safety, maintaining uninterrupted service delivery

BY STEVE BORNHOFT

Businesses across the country and worldwide have confronted unprecedented circumstances and challenges presented by the COVID-19 pandemic.

For Florida Cancer Specialists (FCS), crisis response was especially critical given the indispensable nature of the care and services that it provides and the fact that many patients, due to age and underlying compromising conditions, are highly vulnerable to the virus' effects.

While FCS team members had never conducted tabletop scenarios specifically related to a pandemic, former COO & current Senior Advisor Todd Schonherz says the extensive Emergency Response Plan that had been deployed numerous times during tropical storms and hurricanes proved valuable in addressing three priorities: keeping patients safe, keeping employees safe and providing uninterrupted service.

With this framework, an interdisciplinary team used what he described as a "very methodical approach, functional area by functional area."

Safety the top priority

At the start, swift action was taken to reduce possible transmission and to keep patients and staff safe while continuing to provide care with minimal disruption.

Patient appointments that could be postponed, such as annual follow-ups, were rescheduled. Temperature checks and screening questionnaires were implemented at clinic entrances. And FCS adopted a policy restricting visitors to only the most essential caregivers and delivery personnel.

The use of masks, gowns, hand sanitizers and sanitizing wipes became standard operating procedure.

Chairs and equipment were spaced to provide for social distancing. Protective plastic shields were installed in patient registration and treatment areas. To the extent possible, paper — including forms, informational materials and even magazines in waiting rooms — was eliminated.

The launch of Telehealth services

One of the biggest things FCS did was to stand up a solution for our physicians to conduct telehealth visits with patients. Within 72 hours, a platform was built.

Using video chat, FCS physicians and other care providers are able to consult with patients remotely, enabling convenient and continued access to care from home. FCS personnel had conducted more than 40,000 telehealth visits as of early October, and that number continues to rise.

Transitioning from office to home

Within one week's time, FCS transitioned over 800 office employees to work from home, providing the necessary equipment, connectivity and support to make it nearly seamless.

"A big part of the reason we were able to make these adjustments so quickly," Schonherz said, "was the investment FCS has made in IT infrastructure that was originally designed around disaster recovery from hurricanes."

As the impact of COVID started to take effect, FCS initially extended up to two weeks of paid emergency sick leave to all employees for COVID-related reasons. This was to assist those that needed to make alternate arrangements for the care of their children or other loved ones.

FCS staff were kept apprised of pandemic-related developments and protocols through Daily COVID-19 Update emails. Information was shared continuously with patients as well, through social media, FLCancer.com, office signage and custom messages added into appointment reminder calls.

High marks for FCS response

Patients have been overwhelmingly pleased with FCS efforts. In a recent survey of over 3,000 patients, conducted by an outside organization following their most recent visits, 96% said they were very satisfied with the responsiveness they have received from FCS throughout the pandemic.

In a recent pulse survey, FCS employees, over 81%, reported that they, too, are very satisfied with FCS' response to COVID-19, particularly in the areas of support to those working remotely, protocols to ensure safety and communications.

What is the single most acute challenge your responsibility area has experienced due to the COVID-19 pandemic?

Vicki Caraway, RN, BSN, MBA, ND-BC

Vice President of Clinical Services

The biggest challenge was navigating the information about COVID-19 in a timely manner and making sure that we were using the most up-to-date information to inform our decisions around keeping our patients and staff safe.

We instituted a COVID-19 emergency management team with key leaders in our organization. My role was to manage the creation and communication of policies and procedures necessary to keep everyone safe. I partnered with leaders in all of my respective areas and relied on their expertise to inform our overall strategies for implementation and communication.

In my 30-plus years in healthcare, I have never worked with a more professional and dedicated team. The level of support and engagement far exceeded my expectations. We all burned the midnight oil and just got it done. Every single person took the safety of our patients, visitors and team members to heart, and our mission became one.

By using a multi-disciplinary approach, we were able to cover a lot of ground quickly and to remain nimble as is proving necessary in this rapidly evolving situation.

Paul Chadwick

Chief Procurement Officer

The scale of the shortages of personal protective equipment was staggering early on. All medical supply companies were caught off guard by both the increase in demand and a sharp drop in supply. Our main suppliers put us on a weekly allocation for many products and informed us that they would not get inventory for some items "for months."

The first few weeks were spent trying to find other sources and also trying to predict what would run out next.

The team's work on evaluating all the different vendors, making smart purchasing decisions, and then processing and shipping bulk orders from our warehouse location to clinics has been inspiring.

We are now past the worst shortages. While we are getting a regular supply, we have also been planning for potential future supply interruptions.

Mark Moch

Chief Information Officer

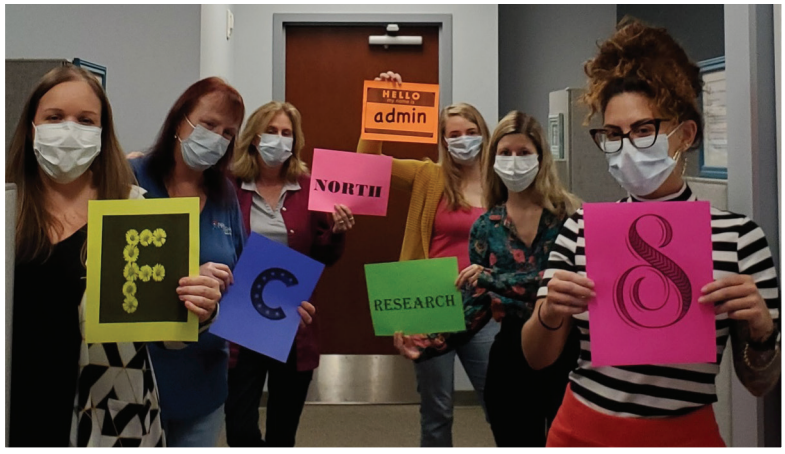
A lot changed for everyone very quickly; the entire IT department understood the sense of urgency.

On the clinical side, making sure our patients were taken care of was most important for us. We were able to quickly address opportunities to maintain the continuum of care through the use of telemedicine. Leveraging our internal resources, we had everything ready to start serving our patients in a very short period of time. Within days, we trained over 600 physicians and care providers and successfully rolled out our platform.

We also had to support the move of over 800 employees from offices to home settings and not skip a beat. We had to secure equipment, create documentation, launch a portal, train users and make sure our system was capable to support the volume of staff working from home. Every task was important.

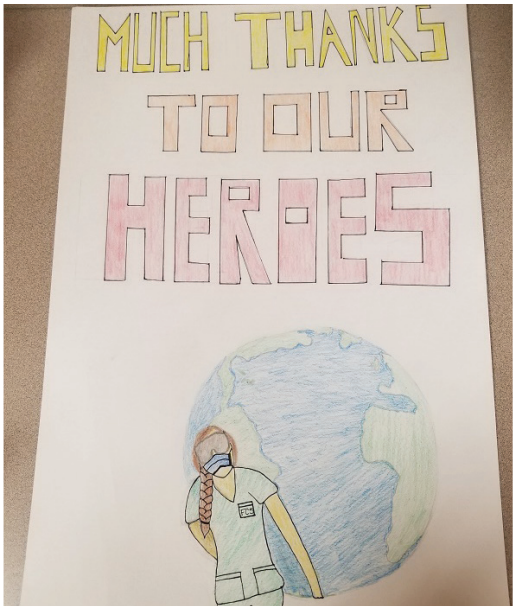
Balancing all of those challenges at the same time and making sure we were not forgetting any critical piece of operation in a very rapidly changing environment was the biggest challenge. It speaks volumes about how dedicated and hardworking our IT organization is.

Since the start of the COVID-19 pandemic, *we've been deeply touched by the thoughtful gestures and acts of kindness received from our patients and community neighbors. We've been equally impressed with the positivity of our dedicated team members. Please enjoy this gallery spotlighting these special moments. We are in this together, every step of the way.*




We Love you
FCS


Our Patients Can't Stay Home
#fcseverystep


MUCH THANKS TO OUR HEROES


SARAH CANNON
FLORIDA CANCER SPECIALISTS


thank you

TELEHEALTH

Florida Cancer Specialists Among the First to Bring Virtual Healthcare to Oncology Patients

BY AUDREY POST

The measures enacted to slow the spread of COVID-19 have been challenging for many healthcare providers. For Florida Cancer Specialists (FCS) physicians and staff, the pandemic has provided the opportunity to expand into telehealth care on a large scale.

"Even before the COVID-19 crisis, we were focused on meeting and exceeding our patients' experiences," said Dr. Lucio Gordan, FCS president and managing physician. "Telehealth has remained largely untapped in cancer care, and COVID-19 is far from over. Whoever can be at home safe, should be."

Patients undergoing cancer treatment are particularly vulnerable, so being able to see a doctor, nutritionist or clinical social worker via video chat provides continuity of care, Gordan said, and it is a change for the better.

"Some patients drive 30 to 60 miles to see a doctor in person, so telemedicine keeps them safe from the spread of illness," he said. "We're able to see them, to review lab results and discuss any problems or issues."

One of the best things about telemedicine, Gordan said, is that it allows more time with patients.

"We're often able to conduct telemedicine when more convenient for the patients' and healthcare providers' busy schedules," he said. "It's less rushed, more flexible; because we tailor the appointment times when office flow is less intense. It's also novel and somewhat more interesting to patients at their home environment, so all are more relaxed."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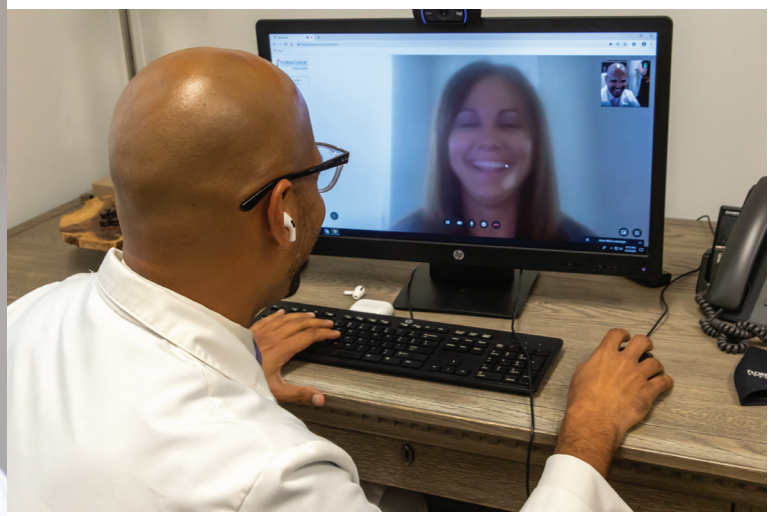

Raul Storey, MD utilizes telehealth to ensure continuity of care with his patients.

'A HUGE UNDERTAKING'

When the decision was made in mid-March to launch telemedicine, the project kicked into high gear immediately, said FCS Chief Information Officer Mark Moch.

"It was a huge undertaking in a very short period of time," he said. "Within one week, we had trained more than 600 people on the system, conducting 120 training sessions and 20 webinars."

That work included building all the documentation for the telehealth solution, including creating how-to guides for FCS providers and for patients. As difficult as it would have been to accomplish while collaborating in traditional workspaces, all this had to be done remotely, because most FCS staff transitioned to working from home since the pandemic began.

"We focused on selecting a solution that would be easy for our patients," Moch said. The technology we selected does not require an app or additional software installation. Connection is established with a simple click of a link that the patient receives via text or email."

As of October, there had been more than 40,000 telehealth visits with FCS patients, Moch said.

The telehealth system will be soon integrated with existing systems within the FCS network, so data can move seamlessly. It is encrypted, so communication between the patient and the physician is secure.

Moch praised the efforts of colleagues in multiple other departments who worked "around the clock" in creating the integrated systems, particularly the Integrated Clinical Services Staff, IT Service Delivery and Revenue Cycle and Operations teams.

Dr. Gordan agreed.

"It has been a great benefit," he said. "Our mission is to deliver world-class care that's close to home. The technology allows us to embrace the future."

Dr. Lucio Gordan
President & Managing Physician

Mark Moch
Chief Information Officer

TELEHEALTH ENHANCES CARE MANAGEMENT

The skilled Care Management team of 170 strong across the FCS network provides vital support and resources to patients as they navigate the many aspects of their care.

The rollout of telemedicine has been an especially helpful tool for behavioral health therapists and oncologist nutritionists and their patients.

"For therapy, you think of someone sitting next to you," said Beth Wittmer, RN, OCN, FCS director of care management. "Patients often feel more comfortable talking from the privacy of their own homes."

In the first two months after the telehealth rollout, nutritionists made 867 virtual visits, and therapists made about 700, she said.

Beth Wittmer
RN, BSN, OCN
Director of Care Management

Nurses have been using telehealth via telephone for about five years, Wittmer said. Each patient has an assigned nurse, and there are nurses on call 24 hours a day if a patient needs to call.

"If there's a silver lining to COVID-19, it's the expansion of telemedicine that will help us continue to improve continuity of care," Wittmer said.

— By Audrey Post

DIRECTOR OF OCCUPATIONAL HEALTH

Navigating the Coronavirus Pandemic

BY KARI C. BARLOW

When she joined Florida Cancer Specialists in February 2019 as its first-ever director of occupational health, Karen Pitman never imagined that a global pandemic would soon be one of her challenges. But that's exactly what happened 13 months later when the coronavirus began spreading across the United States.

For Karen, an experienced, no-nonsense nurse practitioner who loves her job, those first few weeks were a whirlwind of stress and uncertainty.

With responsibility for nearly 100 locations and 4,300 employees across the state, Karen, along with nursing and all other departments, immediately began prioritizing to ensure all needs were met.

Adhering to guidelines from the CDC and other state and federal agencies, keeping patients and employees safe became paramount.

Everyone needed to stay informed and flexible, and everyone in the organization, no matter their job, had a role to play, Karen said.

"We implemented strict infection control protocols immediately and began screenings twice daily on all employees," she said. We mirrored the same process for patients upon entry."

"Ensuring workplace safety and wellness is a significant responsibility for occupational health professionals under normal circumstances," said Joyce Nelson, Chief Human Resources Officer. "The fast paced trajectory of the COVID-19 pandemic has required the continuous development of policies and protocols and attention to countless details to keep FCS a safe place to work and to receive care. Karen has done a remarkable job with her special blend of expertise, fortitude and compassion."

As schools began to shut down across Florida to stem the spread of the virus, it became clear that employees with childcare and other dependent care issues soon would become a top priority for FCS. Next came the need to accommodate hundreds of employees who would be sent home to work remotely under the state's shelter-in-place guidelines.

Add to that the daily challenge of securing enough PPE for employees and implementing new infection control policies, all team members were perpetually in motion. It was a highly integrated process of caring for our patients while also caring for our employees.

"There were many 12- and 14-hour days," Karen said. "Not just for me but also for the administrative and clinic staff." Karen's personal motto, 'I bounce,' keeps the mother of five grown daughters going. "You hit a low or a bump — and then you take a deep breath and dive back in," she says.

Not once did she doubt that FCS was up to the challenge. She acknowledges that it's been a learning process for the entire organization.

"It's probably one of the best teams I've ever worked with," said Karen, who lives in Tampa with her husband, Tom. "From the executive team down, the support we receive is fantastic."

As Karen looks to the future, she predicts that the need for masks, PPE and social distancing will remain critical as the coronavirus continues to spread. "It's such an infectious disease," she said. "I think it's going to stay around for a while."

"I am confident and hopeful," she said. "This is a new norm for everybody. We're just going to have to continue learning and have the stamina to keep going in an ever-changing environment."

"I am confident and hopeful. This is a new norm for everybody. We're just going to have to continue learning and have the stamina to keep going in an ever-changing environment."

DRUG REVIEW

INREBIC® (fedratinib) capsules 100 mg

A Treatment Option for Patients with Intermediate-2 or High Risk Myelofibrosis

Ralph V. Boccia, MD, FACP, is board certified in hematology, medical oncology and internal medicine by the American Board of Internal Medicine. He practices out of the Center for Cancer and Blood Disorders, an AON practice of which he is the founder and medical director, located in Bethesda, Maryland and Germantown, Maryland.

Dr. Boccia is a clinical associate professor of medicine at Georgetown University.

This promotional article was created and funded by Bristol Myers Squibb Company. Dr. Boccia was compensated by Bristol Myers Squibb Company for his participation.

INDICATION

INREBIC® (fedratinib) is indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

IMPORTANT SAFETY INFORMATION

WARNING: ENCEPHALOPATHY INCLUDING WERNICKE'S

Serious and fatal encephalopathy, including Wernicke's, has occurred in patients treated with INREBIC. Wernicke's encephalopathy is a neurologic emergency. Assess thiamine levels in all patients prior to starting INREBIC, periodically during treatment, and as clinically indicated. Do not start INREBIC in patients with thiamine deficiency; replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately discontinue INREBIC and initiate parenteral thiamine. Monitor until symptoms resolve or improve and thiamine levels normalize.

WARNINGS AND PRECAUTIONS

Encephalopathy, including Wernicke's: Serious and fatal encephalopathy, including Wernicke's encephalopathy, has occurred in INREBIC-treated patients. Serious cases were reported in 1.3% (8/608) of patients treated with INREBIC in clinical trials and 0.16% (1/608) of cases were fatal.

Wernicke's encephalopathy is a neurologic emergency resulting from thiamine (Vitamin B1) deficiency. Signs and symptoms of Wernicke's encephalopathy may include ataxia, mental status changes, and ophthalmoplegia (e.g., nystagmus, diplopia). Any change in mental status, confusion, or memory impairment should raise concern for potential encephalopathy, including Wernicke's, and prompt a full evaluation including a neurologic examination, assessment of thiamine levels, and imaging. Assess thiamine levels in all patients prior to starting INREBIC, periodically during treatment, and as clinically indicated. Do not start INREBIC in patients with thiamine deficiency; replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately

The first JAK (Janus kinase) inhibitor for the treatment of myelofibrosis was introduced in 2011.[1,2] In August 2019, the FDA approved the selective JAK2 inhibitor INREBIC (fedratinib) for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis.[3,4] This indication statement is broad; therefore, INREBIC could be an option for patients who are naïve to JAK inhibitors or for patients previously treated with the JAK2 inhibitor ruxolitinib. INREBIC contains a boxed warning for encephalopathy, including Wernicke's encephalopathy.[4]

The FDA approval of INREBIC was based on the results from the pivotal phase 3 JAKARTA trial in JAK-inhibitor-naïve patients with intermediate-2 or high-risk primary or secondary myelofibrosis with splenomegaly.[3,4] Patients were randomized 1:1:1 to receive INREBIC 500 mg (n=97), 400 mg (n=96), or placebo (n=96) once daily for at least 6 cycles. Patients continued to receive INREBIC as long as they were having clinical benefit, defined as complete or partial remission, clinical improvement, or stable disease, and had not experienced disease progression or relapse (as defined by the modified IWG-MRT criteria) or unacceptable toxicity requiring discontinuation. Crossover from the placebo arm was allowed after the randomization period, and crossover patients were randomized 1:1 to one of the 2 INREBIC arms. The primary endpoint was the proportion of patients achieving ≥35% reduction from baseline in spleen volume at the end of cycle 6 as measured by MRI or CT and confirmed with a scan 4 weeks later. The main secondary endpoint was the proportion of patients achieving ≥50% reduction from baseline to the end of cycle 6 in Total Symptom Score (TSS) as measured by the MF-SAF v2.0 diary, which captures the 6 core symptoms of MF: night sweats, itching, abdominal discomfort, early satiety, pain under ribs on left side, and bone or muscle pain.[4,5]

In the intent-to-treat population, 37% (35 of 96) of patients receiving the FDA-approved dose of 400 mg once daily achieved the primary endpoint of ≥35% reduction from baseline in spleen volume at the end of cycle 6 as measured by MRI or CT and confirmed with a scan 4 weeks later. The median duration of the spleen response was 18.2 months. In the placebo arm, one patient (1%) had a spleen volume reduction of ≥35%. In the symptom evaluable population, 40% (36 of 89) of patients in the INREBIC 400 mg arm and 9% (7 of 81)

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discontinue INREBIC and initiate parenteral thiamine. Monitor until symptoms resolve or improve and thiamine levels normalize.

Anemia: New or worsening Grade 3 anemia occurred in 34% of INREBIC-treated patients. The median time to onset of the first Grade 3 anemia was approximately 2 months, with 75% of cases occurring within 3 months. Mean hemoglobin levels reached nadir after 12 to 16 weeks with partial recovery and stabilization after 16 weeks. Red blood cell transfusions were received by 51% of INREBIC-treated patients and permanent discontinuation of INREBIC occurred due to anemia in 1% of patients. Consider dose reduction for patients who become red blood cell transfusion dependent.

Thrombocytopenia: New or worsening Grade ≥3 thrombocytopenia during the randomized treatment period occurred in 12% of INREBIC-treated patients. The median time to onset of the first Grade 3 thrombocytopenia was approximately 1 month; with 75% of cases occurring within 4 months. Platelet transfusions were received by 3.1% of INREBIC-treated patients. Permanent discontinuation of treatment due to thrombocytopenia and bleeding that required clinical intervention both occurred in 2.1% of INREBIC-treated patients. Obtain a complete blood count (CBC) at baseline, periodically during treatment, and as clinically indicated. For Grade 3 thrombocytopenia with active bleeding or Grade 4 thrombocytopenia, interrupt INREBIC until resolved to less than or equal to Grade 2 or baseline. Restart dose at 100 mg daily below the last given dose and monitor platelets as clinically indicated.

Gastrointestinal Toxicity: Gastrointestinal toxicities are the most frequent adverse reactions in INREBIC-treated patients. During the randomized treatment period, diarrhea occurred in 66% of patients, nausea in 62% of patients, and vomiting in 39% of patients. Grade 3 diarrhea 5% and vomiting 3.1% occurred. The median time to onset of any grade nausea, vomiting, and diarrhea was 1 day, with 75% of cases occurring within 2 weeks of treatment. Consider providing appropriate prophylactic anti-emetic therapy (e.g., 5-HT3 receptor antagonists) during INREBIC treatment. Treat diarrhea with anti-diarrheal medications promptly at the first onset of symptoms. Grade 3 or higher nausea, vomiting, or diarrhea not responsive to supportive measures

in the placebo arm had a ≥50% reduction in TSS at the end of cycle 6. In the JAKARTA trial, the most common adverse reactions (reported in ≥20% of patients) included diarrhea (66%), nausea (62%), vomiting (39%), and anemia (40%). Serious adverse reactions occurred in 21% of patients, and included cardiac failure (5%) and anemia (2%). INREBIC was associated with hematologic laboratory abnormalities, such as anemia (74%), thrombocytopenia (47%), and neutropenia (23%).[4]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend fedratinib as initial therapy (category 2B) for patients with intermediate-2 or high-risk myelofibrosis and platelet count ≥50 × 10^9/L and who are transplant ineligible.[6]

It is important to note that INREBIC has a boxed warning for encephalopathy, including Wernicke's. Serious encephalopathy, including Wernicke's, occurred in 8 out of 608 patients in the development program, one of whom had a fatal outcome. Wernicke's is a neurologic emergency resulting from thiamine (vitamin B) deficiency. As such, it is important to assess thiamine levels in all patients prior to starting INREBIC and periodically during treatment as clinically indicated. INREBIC should not be started in patients with thiamine deficiency, and thiamine should be repleted prior to treatment initiation.[4]

In addition to the pivotal study, there was a single-arm phase 2 study in patients who were previously treated with ruxolitinib. The JAKARTA2 study was prematurely terminated, which therefore impacts the interpretability of the data. No conclusions can be drawn regarding the benefit or risk of INREBIC in this patient population and these data are not in the INREBIC label. The JAKARTA2 study included 97 patients with primary or secondary myelofibrosis who were resistant or intolerant to ruxolitinib per investigator assessment. The primary endpoint was the proportion of patients achieving ≥35% reduction from baseline in spleen volume at the end of Cycle 6. Median exposure to ruxolitinib prior to enrollment in the study was 10.7 months. Median exposure to INREBIC during the study was 24 weeks. 30.9% of patients had a confirmed spleen reduction of ≥35% from baseline at the end of Cycle 6 and 26.7% had ≥50% reduction in TSS from baseline at the end of Cycle 6. In patients previously treated with ruxolitinib, hematologic adverse events were observed, including anemia (99.0%), thrombocytopenia (70.1%), and neutropenia (24.0%). The most common (selected)

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within 48 hours, interrupt INREBIC until resolved to Grade 1 or less or baseline. Restart dose at 100 mg daily below the last given dose. Monitor thiamine levels and replete as needed.

Hepatic Toxicity: Elevations of ALT and AST (all grades) during the randomized treatment period occurred in 43% and 40%, respectively, with Grade 3 or 4 in 1% and 0%, respectively, of INREBIC-treated patients. The median time to onset of any grade transaminase elevation was approximately 1 month, with 75% of cases occurring within 3 months. Monitor hepatic function at baseline, periodically during treatment, and as clinically indicated. For Grade 3 or higher ALT and/or AST elevations (greater than 5 × ULN), interrupt INREBIC dose until resolved to Grade 1 or less or to baseline. Restart dose at 100 mg daily below the last given dose. If re-occurrence of a Grade 3 or higher elevation of ALT/AST, discontinue treatment with INREBIC.

Amylase and Lipase Elevation: Grade 3 or higher amylase 2% and/or lipase 10% elevations developed in INREBIC-treated patients. The median time to onset of any grade amylase or lipase elevation was 15 days, with 75% of cases occurring within 1 month of starting treatment. One patient developed pancreatitis in the fedratinib clinical development program (n=608) and pancreatitis resolved with treatment discontinuation. Monitor amylase and lipase at baseline, periodically during treatment, and as clinically indicated. For Grade 3 or higher amylase and/or lipase elevations, interrupt INREBIC until resolved to Grade 1 or less or to baseline. Restart dose at 100 mg daily below the last given dose.

ADVERSE REACTIONS:

The most common adverse reactions for INREBIC treated vs. placebo were diarrhea (66% vs. 16%), nausea (62% vs. 15%), anemia (40% vs. 14%), and vomiting (39% vs. 5%). Dosage interruptions due to an adverse reaction during the randomized treatment period occurred in 21% of patients who received INREBIC. Adverse reactions requiring dosage interruption in >3% of patients who received INREBIC included diarrhea and nausea. Dosage reductions due to an adverse reaction during the randomized treatment period occurred in 19% of patients who received INREBIC. Adverse reactions requiring dosage reduction in >2% of patients who received INREBIC included anemia (6%), diarrhea (3%), vomiting (3%), and thrombocytopenia (2%).

adverse reactions (reported in >30% of patients) included increased creatinine (74.2%), diarrhea (61.9%), nausea (55.7%), increased AST and ALT (47.4% and 45.4%, respectively), and vomiting (41%).[7]

The NCCN Guidelines® also recommend fedratinib (category 2A) for patients with intermediate-2 or high-risk myelofibrosis previously treated with ruxolitinib with no response or loss of response and who have platelet count ≥50 × 10^9/L and who are transplant ineligible.[6] It is important to remember that this guideline should be considered with the following limitations: JAKARTA2, a phase-2, single-arm, open-label study, was prematurely terminated, which impacts the interpretability of the data. No conclusions regarding the benefits or risks of fedratinib in patients who are resistant or intolerant to ruxolitinib can be established based on this study. These data are not included in the Prescribing Information. It is important to assess the patient and the available data before making a decision on what is right for your patient.

Please see Important Safety Information and accompanying Brief Summary, including Boxed WARNING, for INREBIC.

References

1. Bose P, Verstovsek S. Developmental Therapeutics in Myeloproliferative Neoplasms. *Clin Lymphoma Myeloma Leuk*. 2017;17 suppl:S43-S52.
2. Kaplan JB, Stein BL, McMahon B, Giles FJ, Platanias LC. Evolving Therapeutic Strategies for the Classic Philadelphia-Negative Myeloproliferative Neoplasms. *EBioMedicine*. 2016;3:17-25.
3. Celgene Corporation. U.S. FDA Approves INREBIC® (Fedratinib) as First New Treatment in Nearly a Decade for Patients With Myelofibrosis [press release]. https://ir.celgene.com/press-releases-archive/press-release-details/2019/US-FDA-Approves-INREBIC-Fedratinib-as-First-New-Treatment-in-Nearly-a-Decade-for-Patients-With-Myelofibrosis/default.aspx. Accessed February 19, 2020.
4. INREBIC® [package insert]. Summit, NJ: Celgene Corporation; 2019.
5. Pardanani A, Harrison C, Cortes JE, et al. Safety and Efficacy of Fedratinib in Patients With Primary or Secondary Myelofibrosis. *JAMA Oncol*. 2015;1(5):643-651.
6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms V.1.2020. © National Comprehensive Cancer Network, Inc 2020. All rights reserved. Accessed May 21, 2020. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaimers any responsibility for their application or use in any way.
7. Harrison CN, Schaap N, Vannucchi AM, et al. Fedratinib in patients with myeloproliferative neoplasm-associated myelofibrosis previously treated with ruxolitinib: a reanalysis of the phase II JAKARTA-2 study. Presented at 2019 ASCO Annual Meeting; May 31- June 4, 2019; Chicago, IL. Abstract 7057.

DRUG INTERACTIONS:

Coadministration of INREBIC with a strong CYP3A4 inhibitor increases fedratinib exposure. Increased exposure may increase the risk of adverse reactions. Consider alternative therapies that do not strongly inhibit CYP3A4 activity. Alternatively, reduce the dose of INREBIC when administering with a strong CYP3A4 inhibitor. Avoid INREBIC with strong and moderate CYP3A4 inducers. Avoid INREBIC with dual CYP3A4 and CYP2C19 inhibitor. Coadministration of INREBIC with drugs that are CYP3A4 substrates, CYP2C19 substrates, or CYP2D6 substrates increases the concentrations of these drugs, which may increase the risk of adverse reactions of these drugs. Monitor for adverse reactions and adjust the dose of drugs that are CYP3A4, CYP2C19, or CYP2D6 substrates as necessary when coadministered with INREBIC.

PREGNANCY/LACTATION:

Consider the benefits and risks of INREBIC for the mother and possible risks to the fetus when prescribing INREBIC to a pregnant woman. Due to the potential for serious adverse reactions in a breastfed child, advise patients not to breastfeed during treatment with INREBIC, and for at least 1 month after the last dose.

RENAL IMPAIRMENT:

Reduce INREBIC dose when administered to patients with severe renal impairment. No modification of the starting dose is recommended for patients with mild to moderate renal impairment. Due to potential increase of exposure, patients with preexisting moderate renal impairment require more intensive safety monitoring, and if necessary, dose modifications based on adverse reactions.

HEPATIC IMPAIRMENT:

Avoid use of INREBIC in patients with severe hepatic impairment.

Please see accompanying Brief Summary, including Boxed WARNING.

INREBIC® [fedratinib], Capsules for oral use

The following is a Brief Summary; refer to full Prescribing Information for complete product information.

WARNING: ENCEPHALOPATHY INCLUDING WERNICKE'S

Serious and fatal encephalopathy, including Wernicke's, has occurred in patients treated with INREBIC. Wernicke's encephalopathy is a neurologic emergency. Assess thiamine levels in all patients prior to starting INREBIC, periodically during treatment, and as clinically indicated. Do not start INREBIC in patients with thiamine deficiency; replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately discontinue INREBIC and initiate parenteral thiamine. Monitor until symptoms resolve or improve and thiamine levels normalize *[see Dosage and Administration (2.6), Warnings and Precautions (5.1) and Adverse Reactions (6.1)]*.

1 INDICATIONS AND USAGE

INREBIC® (fedratinib) is indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

Conduct baseline testing of thiamine (Vitamin B1) levels prior to initiation of INREBIC *[see Dosage and Administration (2.2), Warnings and Precautions (5.1)]*.

The recommended dosage of INREBIC is 400 mg taken orally once daily for patients with a baseline platelet count of greater than or equal to 50 x 10^9/L.

INREBIC may be taken with or without food. Administration with a high fat meal may reduce the incidence of nausea and vomiting.

Modify the dose for patients using concomitant strong CYP3A4 inhibitors, and in patients with severe renal impairment (creatinine clearance (CL_{cr}) 15 mL/min to 29 mL/min) *[see Dosage and Administration (2.3, 2.4)]*.

If a dose of INREBIC is missed, the next scheduled dose should be taken the following day.

Patients that are on treatment with ruxolitinib before the initiation of INREBIC must taper and discontinue according to the ruxolitinib prescribing information.

2.2 Monitoring for Safety

Obtain the following blood tests prior to starting treatment with INREBIC, periodically during treatment, and as clinically indicated *[see Warnings and Precautions (5.1, 5.2, 5.4, 5.5)]*:

- Thiamine (Vitamin B1) level
- Complete blood count with platelets
- Creatinine and BUN
- Hepatic panel
- Amylase and lipase

2.3 Dose Modifications with Concomitant Use of Strong CYP3A4 Inhibitors

Reduce INREBIC dose when administering with strong CYP3A4 inhibitors to 200 mg once daily.

In cases where co-administration with a strong CYP3A4 inhibitor is discontinued, INREBIC dosage should be increased to 300 mg once daily during the first two weeks after discontinuation of the CYP3A4 inhibitor, and then to 400 mg once daily thereafter as tolerated *[see Drug Interactions (7.1)]*.

2.4 Dose Modifications for Severe Renal Impairment

Reduce INREBIC dose to 200 mg once daily in patients with severe renal impairment (creatinine clearance (CL_{cr}) 15 mL/min to 29 mL/min as estimated by Cockcroft-Gault (C-G) equation).

2.5 Dose Modifications for Adverse Reactions

Modify dose for hematologic and non-hematologic adverse reactions per Table 1 and Table 2. Discontinue INREBIC in patients unable to tolerate a dose of 200 mg daily. See Warnings and Precautions for other mitigating strategies.

Table 1: Dose Modifications for Hematologic Adverse Reactions

Hematologic Adverse Reactions	Dose Reduction
Grade 4 Thrombocytopenia or Grade 3 Thrombocytopenia with active bleeding	Interrupt dose until resolved to Grade 2 or lower or baseline. Restart dose at 100 mg daily below the last given dose.
Grade 4 Neutropenia	Interrupt dose until resolved to Grade 2 or lower or baseline. Restart dose at 100 mg daily below the last given dose.

Consider dose reductions for patients who become transfusion-dependent during treatment with INREBIC.

Table 2: Dose Reductions for Non-hematologic Adverse Reactions

Non-hematologic Adverse Reactions	Dose Reduction
Grade 3 or higher Nausea, Vomiting, or Diarrhea not responding to supportive measures within 48 hours	Interrupt dose until resolved to Grade 1 or lower or baseline. Restart dose at 100 mg daily below the last given dose.
Grade 3 or higher ALT, AST, or Bilirubin	Interrupt dose until resolved to Grade 1 or lower or baseline. Restart dose at 100 mg daily below the last given dose. Monitor ALT, AST, and bilirubin (total and direct) more frequently following the dose reduction. If re-occurrence of a Grade 3 or higher elevation, discontinue treatment with INREBIC.
Grade 3 or higher Other Non-hematologic Toxicities	Interrupt dose until resolved to Grade 1 or lower or baseline. Restart dose at 100 mg daily below the last given dose.

2.6 Management of Thiamine Levels and Wernicke's Encephalopathy (WE)

Assess thiamine levels and nutritional status prior to starting INREBIC and periodically during treatment and as clinically indicated. Do not start INREBIC in patients with thiamine deficiency; replete thiamine prior to treatment initiation and during treatment if thiamine levels are low. If Wernicke's encephalopathy is suspected, immediately discontinue treatment with INREBIC and initiate parenteral thiamine treatment. Monitor until symptoms resolve or improve and thiamine levels normalize *[see Warnings and Precautions (5.1) and Adverse Reactions (6.1)]*.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Encephalopathy, Including Wernicke's

Serious and fatal encephalopathy, including Wernicke's encephalopathy, has occurred in INREBIC-treated patients. Serious cases were reported in 1.3% (8/608) of patients treated with INREBIC in clinical trials and 0.16% (1/608) of cases were fatal.

Wernicke's encephalopathy is a neurologic emergency resulting from thiamine (Vitamin B1) deficiency. Signs and symptoms of Wernicke's encephalopathy may include ataxia, mental status changes, and ophthalmoplegia (e.g., nystagmus, diplopia). Any change in mental status, confusion, or memory impairment should raise concern for potential encephalopathy, including Wernicke's, and prompt a full evaluation including a neurologic examination, assessment of thiamine levels, and imaging. Assess thiamine levels in all patients prior to starting INREBIC, periodically during treatment, and as clinically indicated. Do not start INREBIC in patients with thiamine deficiency; replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately discontinue INREBIC and initiate parenteral thiamine. Monitor until symptoms resolve or improve and thiamine levels normalize *[see Dosage and Administration (2.6) and Clinical Trials Experience (6.1)]*.

5.2 Anemia and Thrombocytopenia

Treatment with INREBIC can cause anemia and thrombocytopenia.

Anemia

New or worsening Grade 3 anemia occurred in 34% of INREBIC-treated patients. The median time to onset of the first Grade 3 anemia was approximately 2 months, with 75% of cases occurring within 3 months. Mean hemoglobin levels reached nadir after 12 to 16 weeks with partial recovery and stabilization after 16 weeks. Red blood cell transfusions were received by 51% of INREBIC-treated patients and permanent discontinuation of INREBIC occurred due to anemia in 1% of patients. Consider dose reduction for patients who become red blood cell transfusion dependent *[see Dosage and Administration (2.5)]*.

Thrombocytopenia

New or worsening Grade ≥3 thrombocytopenia during the randomized treatment period occurred in 12% of INREBIC-treated patients. The median time to onset of the first Grade 3 thrombocytopenia was approximately 1 month; with 75% of cases occurring within 4 months. Platelet transfusions were received by 3.1% of INREBIC-treated patients. Permanent discontinuation of treatment due to thrombocytopenia and bleeding that required clinical intervention both occurred in 2.1% of INREBIC-treated patients.

Obtain a complete blood count (CBC) at baseline, periodically during treatment, and as clinically indicated. For Grade 3 thrombocytopenia with active bleeding or Grade 4 thrombocytopenia, interrupt INREBIC until resolved to less than or equal to Grade 2 or baseline. Restart dose at 100 mg daily below the last given dose and monitor platelets as clinically indicated *[see Dosage and Administration (2.5)]*.

5.3 Gastrointestinal Toxicity

Gastrointestinal toxicities are the most frequent adverse reactions in INREBIC-treated patients. During the randomized treatment period, diarrhea occurred in 66% of patients, nausea in 62% of patients, and vomiting in 39% of patients. Grade 3 diarrhea and vomiting occurred in 5% and 3.1% of patients, respectively. The median time to onset of any grade nausea, vomiting, and diarrhea was 1 day, with 75% of cases occurring within 2 weeks of treatment.

Consider providing appropriate prophylactic anti-emetic therapy (e.g., 5-HT3 receptor antagonists) during INREBIC treatment. Treat diarrhea with anti-diarrheal medications promptly at the first onset of symptoms. For Grade 3 or higher nausea, vomiting, or diarrhea not responsive to supportive measures within 48 hours, interrupt INREBIC until resolved to Grade 1 or less or baseline. Restart dose at 100 mg daily below the last given dose *[see Dosage and Administration (2.5)]*. Monitor thiamine levels and replete as needed.

5.4 Hepatic Toxicity

Elevations of ALT and AST (all grades) during the randomized treatment period occurred in 43% and 40%, respectively, with Grade 3 or 4 in 1% and 0%, respectively, of INREBIC-treated patients. The median time to onset of any grade transaminase elevation was approximately 1 month, with 75% of cases occurring within 3 months.

Monitor hepatic function at baseline, periodically during treatment, and as clinically indicated. For Grade 3 or higher ALT and/or AST elevations (greater than 5 × ULN), interrupt INREBIC dose until resolved to Grade 1 or less or to baseline. Restart dose at 100 mg daily below the last given dose. If re-occurrence of a Grade 3 or higher elevation of ALT/AST, discontinue treatment with INREBIC *[see Dosage and Administration (2.5)]*.

5.5 Amylase and Lipase Elevation

Grade 3 or higher amylase and/or lipase elevations developed in 2% and 10%, respectively, of INREBIC-treated patients. The median time to onset of any grade amylase or lipase elevation was 15 days, with 75% of cases occurring within 1 month of starting treatment. One patient developed pancreatitis in the fedratinib clinical development program (n=608) and pancreatitis resolved with treatment discontinuation.

Monitor amylase and lipase at baseline, periodically during treatment, and as clinically indicated. For Grade 3 or higher amylase and/or lipase elevations, interrupt INREBIC until resolved to Grade 1 or less or to baseline. Restart dose at 100 mg daily below the last given dose *[see Dosage and Administration (2.5)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Encephalopathy, including Wernicke's *[see Warnings and Precautions (5.1)]*
- Anemia and Thrombocytopenia *[see Warnings and Precautions (5.2)]*
- Gastrointestinal Toxicity *[see Warnings and Precautions (5.3)]*
- Hepatic Toxicity *[see Warnings and Precautions (5.4)]*
- Amylase and Lipase Elevation *[see Warnings and Precautions (5.5)]*

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.

The data in the WARNINGS AND PRECAUTIONS Section 5.1 Encephalopathy, including Wernicke's, reflect exposure to INREBIC as a single agent in 608 patients who received more than one dose (ranging from 30 mg to 800 mg) in Studies JAKARTA, ARD11936, JAKARTA2, ARD12042, ARD12888, TED12037/TED12015, INT12497, and TES13519, of whom 459 were patients with myelofibrosis, including 97 patients previously treated with ruxolitinib. Among the 608 patients receiving INREBIC, the median drug exposure was 37 weeks and the median number of cycles initiated was 9 cycles. Fifty-nine percent of 608 patients were exposed for 6 months or longer and 39% were exposed for 12 months or longer.

Using the dataset described above, the most common adverse reactions in >20% of patients (N=608) were diarrhea, nausea, anemia, vomiting, fatigue, thrombocytopenia, and constipation.

JAKARTA Trial

The safety of INREBIC was evaluated in the randomized treatment period of the JAKARTA trial *[see Clinical Studies (14)]*. Key eligibility criteria included adult patients with intermediate-2 or high-risk primary MF or post-PV MF or post-ET MF with splenomegaly, platelet count ≥50 x 10^9/L, and no splenectomy. Patients received INREBIC at 400 mg daily (n=96) or placebo (n=95). Among patients receiving INREBIC, 82% were exposed for more than 6 months and 65% for more than one year. Patients had a median duration of exposure to INREBIC 400 mg daily of 15.5 months compared with placebo where patients were treated for 6 months or until disease progression after which patients were allowed to crossover to active treatment. The median age of patients who received INREBIC was 65 years (range: 27 to 86 years), 59% were male, 90% were White, 8% were Asian, 1% were Black, 1% were Other, and 92% had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1.

Serious adverse reactions occurred in 21% of INREBIC-treated patients. Serious adverse reactions in ≥2% of patients receiving INREBIC 400 mg daily included cardiac failure (5%) and anemia (2%). Fatal adverse reactions of cardiogenic shock occurred in 1% of patients receiving INREBIC 400 mg daily.

Permanent discontinuation due to an adverse reaction occurred in 14% of patients receiving INREBIC. Most frequent reasons for permanent discontinuation in ≥2% of patients receiving INREBIC included cardiac failure (3%), thrombocytopenia, myocardial ischemia, diarrhea, and increased blood creatinine (2% each).

Dosage interruptions due to an adverse reaction during the randomized treatment period occurred in 21% of patients who received INREBIC. Adverse reactions requiring dosage interruption in >3% of patients who received INREBIC included diarrhea and nausea.

Dosage reductions due to an adverse reaction during the randomized treatment period occurred in 19% of patients who received INREBIC. Adverse reactions requiring dosage reduction in >2% of patients who received INREBIC included anemia (6%), diarrhea (3%), vomiting (3%), and thrombocytopenia (2%).

The most common adverse reactions (reported in ≥20%) were diarrhea, nausea, anemia, and vomiting.

Tables 3 and 4 summarize the common adverse reactions and laboratory abnormalities, respectively, in JAKARTA during randomized treatment.

Table 3: Adverse Reactions Reported in ≥5% Patients Receiving INREBIC 400 mg with a Difference between Arms of >5% during Randomized Treatment

	INREBIC 400 mg (n=96)		Placebo (n=95)	
Adverse Reaction[a]	**All Grades %**	**Grade ≥3[b] %**	**All Grades %**	**Grade ≥3 %**
Diarrhea	66	5	16	0
Nausea	62	0	15	0
Anemia	40	30	14	7
Vomiting	39	3.1	5	0
Fatigue or asthenia	19	5	16	1.1
Muscle spasms	12	0	1.1	0
Blood creatinine increased	10	1	1.1	0
Pain in extremity	10	0	4.2	0
Alanine aminotransferase Increased	9	0	1.1	0
Headache	9	0	1.1	0
Weight increased	9	0	4.2	0
Dizziness	8	0	3.2	0
Bone pain	8	0	2.1	0
Urinary tract infection[c]	6	0	1.1	0
Dysuria	6	0	0	0
Aspartate aminotransferase increased	5	0	1.1	0

[a] CTCAE version 4.03.
[b] Only 1 Grade 4 event (anemia).
[c] Includes cystitis.

Clinically significant adverse reactions reported in 5% or less of patients: hypertension of all grades was reported in 4.2% of patients and Grade 3 or higher in 3% of INREBIC-treated patients.

Changes in selected post-baseline laboratory values that were observed are shown in Table 4 for the JAKARTA trial during randomized treatment.

Table 4: Selected Laboratory Abnormalities That Have Worsened from Baseline (≥20%) in Patients Receiving INREBIC with a Difference between Arms of >10% When Compared to Placebo in JAKARTA during Randomized Treatment

	INREBIC 400 mg (n=96)		Placebo (n=95)	
Laboratory Parameter	**All Grades %**	**Grade ≥3 %**	**All Grades %**	**Grade ≥3 %**
Hematology				
Anemia	74	34	32	10
Thrombocytopenia	47	12	26	10
Neutropenia	23	5	13	3.3
Biochemistry				
Creatinine increased	59	3.1	19	1.1
ALT increased	43	1	14	0
AST increased	40	0	16	1.1
Lipase increased	35	10	7	2.2
Hyponatremia	26	5	11	4.3
Amylase increased	24	2.1	5	0

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on INREBIC

Strong CYP3A4 Inhibitors

Coadministration of INREBIC with a strong CYP3A4 inhibitor increases fedratinib exposure *[see Clinical Pharmacology (12.3)]*. Increased exposure may increase the risk of adverse reactions *[see Warnings and Precautions (5), and Adverse Reactions (6.1)]*. Consider alternative therapies that do not strongly inhibit CYP3A4 activity. Alternatively, reduce the dose of INREBIC when administering with a strong CYP3A4 inhibitor *[see Dosage and Administration (2.3)]*.

Strong and Moderate CYP3A4 Inducers

Avoid INREBIC with strong and moderate CYP3A4 inducers. The effect of concomitant administration of a strong or moderate CYP3A4 inducer with INREBIC has not been studied *[see Clinical Pharmacology (12.3)]*.

Dual CYP3A4 and CYP2C19 Inhibitors

Avoid INREBIC with dual CYP3A4 and CYP2C19 inhibitor. The effect of concomitant administration of a dual CYP3A4 and CYP2C19 inhibitor with INREBIC has not been studied *[see Clinical Pharmacology (12.3)]*.

7.2 Effect of INREBIC on Other Drugs

CYP3A4, CYP2C19, or CYP2D6 Substrate Drugs

Coadministration of INREBIC with drugs that are CYP3A4 substrates, CYP2C19 substrates, or CYP2D6 substrates increases the concentrations of these drugs, which may increase the risk of adverse reactions of these drugs *[see Clinical Pharmacology (12.3)]*. Monitor for adverse reactions and adjust the dose of drugs that are CYP3A4, CYP2C19, or CYP2D6 substrates as necessary when coadministered with INREBIC.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on INREBIC use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of fedratinib to pregnant rats during organogenesis at doses considerably lower than the recommended human daily dose of 400 mg/day resulted in adverse developmental outcomes *(see Data)*. Consider the benefits and risks of INREBIC for the mother and possible risks to the fetus when prescribing INREBIC to a pregnant woman.

The background risk of major birth defects and miscarriage for the indicated population is unknown. Adverse outcomes in pregnancy occur regardless of the health of the mother or the use of medications. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In an embryo-fetal development study in pregnant rats, fedratinib administration at a dose of 30 mg/kg/day during organogenesis (gestation days 6 to 17) was associated with adverse developmental outcomes including skeletal variations (such as additional ossification center of neuronal arches). These effects occurred in rats at approximately 0.1 times the clinical exposure based on AUC at the recommended daily dose. At lower doses of 10 mg/kg/day (0.01 times the clinical exposure at the recommended daily dose), fedratinib administered to pregnant rats resulted in maternal toxicity of decreased gestational weight gain.

In an embryo-fetal development study in pregnant rabbits, fedratinib administration during organogenesis (gestation Days 6 to 18) did not produce developmental or maternal toxicity at doses up to the highest dose level tested, 30 mg/kg/day (approximately 0.08 times the clinical exposure at the recommended daily dose). In a separate study, administration of 80 mg/kg/day fedratinib to rabbits resulted in maternal mortality.

In a pre- and postnatal study in rats, fedratinib was administered to pregnant female rats at doses of 3, 10, or 30 mg/kg/day from Day 6 of gestation through Day 20 of lactation, with weaning on Day 21. A slight decrease in maternal body weight gain during gestation occurred at 30 mg/kg/day. The offspring from the high dose (30 mg/kg) had decreased body weight preweaning in both sexes and postweaning through the maturation phase in males. These effects occurred at exposures approximately 0.1 times the clinical exposure at the recommended daily dose.

8.2 Lactation

Risk Summary

There are no data on the presence of fedratinib or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise patients not to breastfeed during treatment with INREBIC, and for at least 1 month after the last dose.

8.4 Pediatric Use

The safety and effectiveness of INREBIC in pediatric patients have not been established.

8.5 Geriatric Use

Of the total number of patients with myelofibrosis who received an INREBIC dose of 400 mg in the clinical studies, 47.3% were greater than 65 years of age and 12.3% were greater than 75 years of age. No overall differences in safety or effectiveness of INREBIC were observed between these patients and younger patients.

8.6 Renal Impairment

Reduce INREBIC dose when administered to patients with severe renal impairment (CL_{cr} 15 mL/min to 29 mL/min by Cockcroft-Gault) *[see Dosage and Administration (2.4) and Clinical Pharmacology (12.3)]*. No modification of the starting dose is recommended for patients with mild to moderate renal impairment (CLcr 30 mL/min to 89 mL/min by Cockcroft-Gault). Due to potential increase of exposure, patients with pre-existing moderate renal impairment require more intensive safety monitoring, and if necessary, dose modifications based on adverse reactions *[see Dosage and Administration (2.5)]*.

8.7 Hepatic Impairment

INREBIC pharmacokinetics has not been evaluated in patients with severe hepatic impairment (total bilirubin > 3 times ULN and any AST). Avoid use of INREBIC in patients with severe hepatic impairment *[see Clinical Pharmacology (12.3)]*.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Discuss the following with patients prior to and during treatment with INREBIC.

Encephalopathy, including Wernicke's

Advise patients that serious and fatal encephalopathy, including Wernicke's, has occurred in patients taking INREBIC. Wernicke's encephalopathy is a neurological emergency resulting from acute thiamine (Vitamin B1) deficiency. Advise patients of the need to monitor thiamine levels *[see Dosage and Administration (2.1, 2.2, 2.6), and Warnings and Precautions (5.1)]*. Advise patients to seek emergency medical attention for any change in mental status such as confusion, drowsiness or memory impairment, cerebellar abnormalities such as ataxia, and ophthalmic abnormalities such as diplopia and nystagmus. Advise patients to contact their healthcare provider right away if they experience nausea, vomiting, diarrhea, and weight loss unresponsive to treatment resulting in malnutrition and lower thiamine levels, which may lead to Wernicke's encephalopathy *[see Boxed Warning and Warnings and Precautions (5.1)]*.

Anemia and Thrombocytopenia

Advise patients that INREBIC is associated with anemia and thrombocytopenia, and of the need to monitor complete blood counts before and during treatment *[see Warnings and Precautions (5.2)]*.

Gastrointestinal Toxicity

Advise patients to contact their healthcare provider if they experience intractable diarrhea, nausea, or vomiting. Prescribers should advise patients of the potential complications of severe diarrhea, nausea, or vomiting *[see Warnings and Precautions (5.3)]*.

Hepatic Toxicity

Advise patients that INREBIC may increase liver enzymes and of the need to monitor liver enzyme levels *[see Warnings and Precautions (5.4)]*.

Amylase and Lipase Elevation

Advise patients that INREBIC may increase amylase and lipase and of the need to monitor amylase and lipase *[see Warnings and Precautions (5.5)]*.

Lactation

Advise patients not to breastfeed during treatment with INREBIC and for at least 1 month after the final dose *[see Use in Specific Populations (8.2)]*.

Dosing and Storage Instructions

- Instruct patients that if they miss a dose of INREBIC, skip the dose and take it the next day and return to normal schedule *[see Dosage and Administration (2.1)]*. Warn patients not to take 2 doses to make up for the missed dose.

Manufactured for and marketed by:
Celgene Corporation
Summit, NJ 07901

FCS DIRECTOR OF RESEARCH OPERATIONS

Q&A with James Reeves Jr., MD on the importance of clinical trials

In partnership with Sarah Cannon Research Institute, FCS is able to provide our patients with greater opportunities to access cutting-edge therapies. FCS Director of Research Operations Dr. James Reeves Jr. discusses the tremendous importance of clinical trials in cancer treatment.

Why are clinical trials important?

When you think of all the great medicines that we have now and all of the tremendous advances we have made in cancer treatment just in the last 10 years, all of those came about because of clinical trials. Basically, through this step by step process, we compare a new therapy to a standard therapy that we've had before and then the winner becomes the next standard therapy — that's the base for the next clinical trial.

What advancements are being made in clinical trials?

Over the last several years, we've been able to start to dissect why some cancers are different than others and why some patients respond to standard of care therapy and other patients don't. We're beginning to understand the molecular drivers and why every lung cancer or breast cancer is not the same and begin to select treatments that are specific, or targeted, for that individual patient and that patient's cancer to get the best response and the best outcome. This is really the epitome of personalized medicine.

How do clinical trials impact cancer care today and in the future?

These days, if you're a patient, you want to be on a clinical trial because the science has come to the point where it's very unusual to have a research drug that doesn't perform at least as well as standard therapy.

What should people know about clinical trials?

It's very important for people to understand that these trials are overseen by the FDA. There is a very robust consent process that patients go through and participate in to help them understand the anticipated risks and benefits.

A common objection is, "I don't want to be a guinea pig." At the time that they become eligible for a clinical trial, patients are either going to get the best standard therapy that is agreed on by a wide consensus of doctors throughout the world or they are going to get a therapy that we really think is going to be better based on that trial. I think patients need to go through the consent process and see if the trial seems to be a good idea for them. They should feel assured that the degree of oversight is such that they are probably going to do very well regardless of what treatment they are assigned to on the trial.

FCS physicians were the co-authors of 20 research studies presented at the American Society of Clinical Oncology (ASCO) ASCO20 Virtual Scientific Program in May. "We are extremely proud that research done through the FCS Phase 1 Drug Development Units and at FCS clinics throughout Florida, in partnership with Sarah Cannon Research Institute, is contributing so significantly to cancer treatment advances," said Dr. James A. Reeves Jr., director of FCS Research Operations.

FCS Foundation News & Events

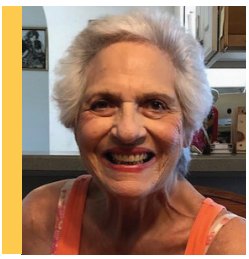
FCS Foundation Goes Virtual to Ensure Safety and Continues to Provide Patient Grants

The challenges of the COVID-19 pandemic have not kept the FCS Foundation team from aiding cancer patients in need.

Working remotely, our staff and dedicated volunteers have continued to accept and process donations and applications and issue grants. Some of the Foundation volunteers, who are usually busy in FCS offices and clinics, now support the Foundation virtually by retrieving phone messages, reviewing grant applications and managing other tasks.

The FCS Foundation continues to develop creative strategies to provide grants without disruption, as you'll see from the stories below:

A NOTE OF APPRECIATION



"When I was diagnosed with Stage 2 lung cancer in January 2019, I thought I was done. Both my husband and I had been out of work for almost two years, and the only income we had was his pension and Social Security. We were behind in mortgage payments but up to date with other bills. I applied to the Foundation with the hope of receiving some financial assistance. I was approved for a grant of $2,000. This grant allowed us to catch up on our mortgage by covering other bills. Working with the Foundation, I found caring, compassionate people who were always there to help and answer questions. I am eternally grateful to the FCS Foundation for helping us through a very difficult time." — Ronni Cucchiara

ACTS OF KINDNESS

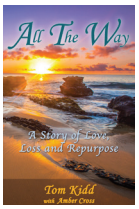
Cynthia McCormick is one of our many dedicated FCS Foundation volunteers assisting us remotely during the pandemic. Recently, she shared her story of how she came to work with the Foundation and her experience helping us virtually:

"Volunteering is a way for me to give back in remembrance of my mother, who was a long-term patient at FCS in Clermont. She loved going there! After she passed, I reflected on this and felt like I wanted to interact with others who were at the clinic and hopefully share some compassion, assistance and comfort — and a smile when needed. Giving back through volunteering enriches my life. So, for now, I'll help from home, and, to quote Winston Churchill, 'Keep calm and carry on.'"

FCS Foundation establishes Joan L. Kidd, MD Memorial Fund

In partnership with Florida resident Tom Kidd, the Florida Cancer Specialists (FCS) Foundation has established the Joan L. Kidd, MD Memorial Fund, which honors Tom's late wife.

A respected internal medicine and family medicine physician, Dr. Kidd was also a two-time Stage IIIC ovarian cancer survivor. All proceeds from the sales of Tom's e-book, "All the Way," a memoir reflecting on the couple's life together and their cancer journey, will be donated to the FCS Foundation to seed the Fund on an ongoing basis and provide grants to cancer patients in need. Tom has also committed to match the first $10,000 of book sales to aid patient support organizations in their fundraising efforts. The memoir is available in e-book format and can be downloaded to all devices. To purchase or learn more, visit FCSF.org.



FLORIDA CANCER SPECIALISTS FOUNDATION WELCOMES NEW BOARD MEMBERS

FCS Foundation Board of Directors named seven (7) additional leaders to join the board.

A board-certified radiation oncologist with over 20 years' experience, **Dr. Cherylle Hayes** is the medical director at North Florida Regional Medical Center.

Dr. Cherylle Hayes

Tom Kidd is the founder and CEO of the Joan L. Kidd, MD Fight for Life Continuum, an initiative he established in 2016, in memory of his late wife to enhance the quality of life for terminal cancer patients.

Tom Kidd

Crystal and Tim O'Donohue are owners of Castle Gate Farm, LLC, the Ocala region's premiere equine center featuring a thoroughbred and equestrian show jumping facility.

Crystal and Tim O'Donohue

A Board-certified medical oncologist, **Dr. Raul Storey** practices at the offices of Florida Cancer Specialists in Vero Beach and Sebastian.

Dr. Raul Storey

Rhonda Webster is the business development manager for Beja Body in Orlando. **David** is a criminal defense lawyer and former prosecutor who is the founder of The Law Office of David A. Webster, P.A., based in Longwood, Florida.

Rhonda and David Webster

TRINITY CANCER CENTER

Construction of our new state-of-the-art FCS Trinity Cancer Center in Pasco County is underway; it will replace our current sites in New Port Richey when it opens in early 2021. With nearly double the amount of space, patients will have convenient access to comprehensive care, including medical oncology, radiation oncology, radiology, laboratory and care management services and clinical trials close to home.

SEBRING CANCER CENTER

FCS recently cut the ribbon on a new state-of-the-art facility at 1396 Whisper Circle in Sebring.
The new location replaces the existing FCS clinic. To enhance patient comfort and convenience, the new, 13,500 square-foot clinic has nearly double the space of the former location and includes 16 private exam rooms and 40 infusion therapy chairs. On-site laboratory testing, as well as PET and CT, are available.

FLORIDA CANCER SPECIALISTS & RESEARCH INSTITUTE WELCOMES JASON COE AS CHIEF OPERATING OFFICER

FCS is pleased to announce that Jason Coe has been named to the Executive Leadership Team as Chief Operating Officer. In this role, he is responsible for the day-to-day operations of the statewide practice, focusing on delivering high-quality, value-based cancer care.

A seasoned executive with nearly 25 years of healthcare experience, Jason has a strong operations background, sharp focus, and demonstrated success driving organizational change. He earned his MBA from the University of Central Florida and a bachelor's degree in business administration from Columbia Union College in Maryland.

Prior to joining FCS, Jason served as the COO of AdventHealth Tampa. His proven track record includes the collaboration of large multi-specialty physician groups comprised of surgical oncology, radiation oncology, urology and OB/GYN. Jason provided executive oversight for the construction of a $250 million surgical tower and the expansion of radiology services, as well as numerous outpatient specialty services. He led the process to achieve Commission on Cancer certification.

WE WELCOME THE FOLLOWING PHYSICIANS

Martin Dietrich, MD, PhD
Medical Oncologist/
Hematologist in
Lake Mary and Oviedo.

Margarett Ellison, MD
Gynecologic Oncologist at Gynecologic Oncology of Tallahassee, A Division of Florida Cancer Specialists.

Raji Shameem, MD
Medical Oncologist/
Hematologist in Deland,
Lake Mary and Oviedo.

Our new FCS office in Middleburg opened on June 1. Patients in the greater Jacksonville area now have a second option, in addition to our Fleming Island location, for receiving care closer to home from Drs. Bubis, Kent and Villegas.

Jeffrey A. Bubis, DO
Medical Oncologist

Elizabeth Kent, MD
Medical Oncologist

Augusto Villegas, MD
Medical Oncologist

From Our Patients

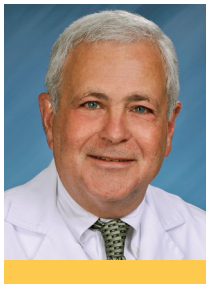
I am very pleased to share with you that Dr. Vivian Griffin and her team – every single member – has treated me with professionalism and competence.

Jean, Casi and Betsy appear to be seasoned, intelligent, compassionate and hard working. I'm impressed by how efficiently they set up the equipment and double check each other on various settings ... I actually enjoy my time with them. Emily has cheerfully jumped through extra hoops to get my prescriptions at lower co-pays and fielding my questions.

In short, I think Dr. Griffin and her radiation team rock! I enjoy interacting with every one of them and am grateful for their efforts to save my life. I will recommend them to everyone.

Have something to add?

You can submit your feedback by emailing us at FCSCommunications@FLCancer.com



Thank you to Dr. Christopher George and his amazing nurse, Lisa, at the Tampa MLK office. I was diagnosed with breast cancer with bone metastasis back in 2014, right before my 40th birthday.

Dr. George, Lisa and the entire staff are the reason I'm still here today. ❤️❤️

Dr. Elizabeth Kent at the Fleming office is incredible! She took her time with me, made sure I was heard and understood everything. She is a wonderful doctor!

I have always had great care from Dr. Marilyn Raymond and her staff since 2007. When my port clotted and had emergency surgery, everyone was attentive and compassionate. Dr. Raymond is the best!

Everyone treats me like I'm special. Dr. Amit Shah takes time to explain my scans and never gives up. The office staff at Sebring is top notch. Thank you.

Show your pride in the power of **community**

The pandemic has amplified the ways a community practice is the best source for patients to receive care close to home. Your business has changed drastically to ensure the safety of patients and staff, but patients may still be reluctant to come in for care.

We take our role as a partner and advocate for community care providers seriously. As such, we are pleased to announce the **#weARECommunity** campaign to help you let patients know – NOW is the time to prioritize health and get back to the doctor.

Follow and like our companies on LinkedIn, Facebook and Twitter and join the conversation.

AmerisourceBergen®

Oncology Supply | ION Solutions | Besse Medical
IPN Solutions | IntrinsiQ Specialty Solutions

#weARECommunity
AmerisourceBergen

Virtual Symposia from ION

ION Solutions is implementing a new educational series, presented on a virtual platform, so that all GPO members will have the opportunity to access highlights from the major national and international meetings without having to leave their home or office.

- Virtual format, with your convenience and safety in mind
- Held on Saturday mornings, once a month, to be respectful of your office hours
- Moderated by ION's Medical Director and Chair of ION's Medical Advisory Panel, Ralph Boccia, MD, FACP
- Faculty comprised of the most renowned experts in their respective fields
- No registration fee, no software to download, no need to travel

Visit IONonline.com to register for these events as they are opened.

Schedule of Virtual Events

2020

October	*Best of ESMO Congress*
November 21	*Highlights of ASCO's Clinical Immuno-Oncology Symposium (SITC)*
December 19	*Best of San Antonio Breast Cancer Symposium*

2021

January 30	*Best of ASCO's Gastrointestinal Cancers Symposium*
February 20	*Best of ASCO's Genitourinary Cancers Symposium*
March 20	*Updates in Precision Medicine*
April 17	*Updates from NCCN Annual Meeting*
May 15	*Highlights from ONS' Annual Congress*
June 12	*Best of ASCO 2021 Part 1*
July 17	*Best of ASCO 2021 Part 2*

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