FALL/WINTER 2021

FCS THE MAGAZINE

Main Motivation

Tarralyn Jones' faith & mindset help her heal

For adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received 2 or more prior systemic therapies, at least one of them for metastatic disease

A WAY IN WITH TRODELVY

TRODELVY attacks mTNBC with an antibody-drug conjugate (ADC) that binds to Trop-2.[1]

Based on preclinical data. May not correlate with clinical outcomes.

EXPLORE MORE POSSIBILITIES. SCAN TO VISIT TRODELVYHCP.COM.

INDICATION

TRODELVY® (sacituzumab govitecan-hziy) is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: NEUTROPENIA AND DIARRHEA

- **Severe or life-threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm³ or neutropenic fever. Monitor blood cell counts periodically during treatment. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patients with febrile neutropenia without delay.**
- **Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. Administer atropine, if not contraindicated, for early diarrhea of any severity. At the onset of late diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold TRODELVY until resolved to ≤Grade 1 and reduce subsequent doses.**

CONTRAINDICATIONS

- Severe hypersensitivity reaction to TRODELVY.

WARNINGS AND PRECAUTIONS

Neutropenia: Severe, life-threatening, or fatal neutropenia can occur and may require dose modification. Neutropenia occurred in 61% of patients treated with TRODELVY. Grade 3-4 neutropenia occurred in 47% of patients. Febrile neutropenia occurred in 7%. Withhold TRODELVY for absolute neutrophil count below 1500/mm³ on Day 1 of any cycle or neutrophil count below 1000/mm³ on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever.

Diarrhea: Diarrhea occurred in 65% of all patients treated with TRODELVY. Grade 3-4 diarrhea occurred in 12% of patients. One patient had intestinal perforation following diarrhea. Neutropenic colitis occurred in 0.5% of patients. Withhold TRODELVY for Grade 3-4 diarrhea and resume when resolved to ≤Grade 1. At onset, evaluate for infectious causes and if negative, promptly initiate loperamide, 4 mg initially followed by 2 mg with every episode of diarrhea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures (e.g., fluid and electrolyte substitution) may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment can receive appropriate premedication (e.g., atropine) for subsequent treatments.

Hypersensitivity and Infusion-Related Reactions: Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 37% of patients. Grade 3-4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.3%. The incidence of anaphylactic reactions was 0.3%. Pre-infusion medication is recommended. Observe patients closely for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Medication to treat such reactions, as well as emergency equipment, should be available for immediate use. Permanently discontinue TRODELVY for Grade 4 infusion-related reactions.

GILEAD

For adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received 2 or more prior systemic therapies, at least one of them for metastatic disease

TRODELVY IMPROVED SURVIVAL IN 2L+ mTNBC

In the phase 3 ASCENT trial*

PROVEN SURVIVAL BENEFIT

In brain metastases-negative (BM-neg) population[2*]

3X LONGER
MEDIAN PFS
than single-agent chemotherapy

5.6 months with TRODELVY (range: 4.3–6.3) (n=235) vs **1.7 months** with single-agent chemotherapy (range: 1.5–2.6) (n=233); 95% CI, HR: 0.41 (0.32–0.52) *P*<.0001

In the full population[1*]

- Median PFS was 4.8 months for TRODELVY (range: 4.1–5.8) (n=267) vs 1.7 months with single-agent chemotherapy (range: 1.5–2.5) (n=262); 95% CI, HR: 0.43 (0.35–0.54) *P*<.0001

In BM-neg population[2*]

1 YEAR
MEDIAN OS

12.1 months with TRODELVY (range: 10.7–14.0) (n=235) vs **6.7 months** with single-agent chemotherapy (range: 5.8–7.7) (n=233); 95% CI, HR: 0.48 (0.38–0.59) *P*<.0001

In the full population[1*]

- Median OS was 11.8 months for TRODELVY (range: 10.5–13.8) (n=267) vs 6.9 months with single-agent chemotherapy (range: 5.9–7.6) (n=262); 95% CI, HR: 0.51 (0.41–0.62) *P*<.0001

***TRODELVY was studied in ASCENT, a phase 3, randomized, active-controlled, open-label trial. Patients were randomized (1:1) to receive TRODELVY 10 mg/kg as an intravenous infusion on Days 1 and 8 of a 21-day cycle (n=267) or physician's choice of single-agent chemotherapy (n=262), which included eribulin, vinorelbine, gemcitabine, or capecitabine. Patients were treated until disease progression or unacceptable toxicity. The efficacy analysis included Progression-Free Survival (PFS) in BM-neg patients (primary endpoint) by BICR based on RECIST 1.1 criteria, PFS for the full population (all patients with and without brain metastases), and Overall Survival (OS) vs single-agent chemotherapy.**

- **88% of the full population were BM-neg.[1] Results in these patients were similar to those seen in the full population (all randomized patients).[2] See exploratory findings for BM-positive population at TRODELVYHCP.com**
- **13% of patients in the TRODELVY group in the full population received only 1 prior line of systemic therapy in the metastatic setting (in addition to having disease recurrence or progression within 12 months of neoadjuvant /adjuvant systemic therapy). Efficacy results for this subgroup of patients were consistent with those who had received at least 2 prior lines in the metastatic setting[1]**

BICR=blinded, independent, central review; CI=confidence interval; HR=hazard ratio; OS=Overall Survival; PFS=Progression-Free Survival; RECIST=Response Evaluation Criteria in Solid Tumors.

TRODELVY™
sacituzumab govitecan-hziy
180 mg for injection

Nausea and Vomiting: Nausea occurred in 66% of all patients treated with TRODELVY and Grade 3 nausea occurred in 4% of these patients. Vomiting occurred in 39% of patients and Grade 3-4 vomiting occurred in 3% of these patients. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK_1 receptor antagonist as well as other drugs as indicated) for prevention of chemotherapy-induced nausea and vomiting (CINV). Withhold TRODELVY doses for Grade 3 nausea or Grade 3-4 vomiting and resume with additional supportive measures when resolved to Grade ≤1. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting.

Increased Risk of Adverse Reactions in Patients with Reduced UGT1A1 Activity: Patients homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk for neutropenia, febrile neutropenia, and anemia and may be at increased risk for other adverse reactions with TRODELVY. The incidence of Grade 3-4 neutropenia was 67% in patients homozygous for the UGT1A1*28, 46% in patients heterozygous for the UGT1A1*28 allele and 46% in patients homozygous for the wild-type allele. The incidence of Grade 3-4 anemia was 25% in patients homozygous for the UGT1A1*28 allele, 10% in patients heterozygous for the UGT1A1*28 allele, and 11% in patients homozygous for the wild-type allele. Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue TRODELVY based on clinical assessment of the onset, duration and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced UGT1A1 function.

Embryo-Fetal Toxicity: Based on its mechanism of action, TRODELVY can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. TRODELVY contains a genotoxic component, SN-38, and targets rapidly dividing cells. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose.

ADVERSE REACTIONS

In the ASCENT study (IMMU-132-05), the most common adverse reactions (incidence ≥25%) were fatigue, neutropenia, diarrhea, nausea, alopecia, anemia, constipation, vomiting, abdominal pain, and decreased appetite. The most frequent serious adverse reactions (SAR) (>1%) were neutropenia (7%), diarrhea (4%), and pneumonia (3%). SAR were reported in 27% of patients, and 5% discontinued therapy due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence ≥25%) in the ASCENT study were reduced neutrophils, leukocytes, and lymphocytes.

DRUG INTERACTIONS

UGT1A1 Inhibitors: Concomitant administration of TRODELVY with inhibitors of UGT1A1 may increase the incidence of adverse reactions due to potential increase in systemic exposure to SN-38. Avoid administering UGT1A1 inhibitors with TRODELVY.

UGT1A1 Inducers: Exposure to SN-38 may be substantially reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY.

References: 1. TRODELVY [package insert]. Foster City, CA: Gilead Sciences, Inc.; April 2021. **2.** Data on file. Gilead Sciences, Inc. 2021.

Please see Brief Summary of full Prescribing Information, including BOXED WARNING, on the next page.

TRODELVY® (sacituzumab govitecan-hziy) for injection, for intravenous use
Brief Summary of full Prescribing Information. See full Prescribing Information. Rx Only.

WARNING: NEUTROPENIA AND DIARRHEA

- **Severe or life-threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Monitor blood cell counts periodically during treatment. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patients with febrile neutropenia without delay.**
- **Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. Administer atropine, if not contraindicated, for early diarrhea of any severity. At the onset of late diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold TRODELVY until resolved to ≤ Grade 1 and reduce subsequent doses.**

[See Warnings and Precautions and Dosage and Administration]

INDICATIONS AND USAGE

*Also see **Clinical Studies***

TRODELVY (sacituzumab govitecan-hziy) is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with:

- Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.
- Locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and either programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

DOSAGE AND ADMINISTRATION

*Also see **Warnings and Precautions***

Do NOT substitute TRODELVY for or use with other drugs containing irinotecan or its active metabolite SN-38.

The recommended dose of TRODELVY is 10 mg/kg administered as an intravenous infusion once weekly on Days 1 and 8 of 21-day treatment cycles. Continue treatment until disease progression or unacceptable toxicity. Do not administer TRODELVY at doses greater than 10 mg/kg. Administer TRODELVY as an intravenous infusion only. Do not administer as an intravenous push or bolus.

- First infusion: Administer infusion over 3 hours. Observe patients during the infusion and for at least 30 minutes following the initial dose, for signs or symptoms of infusion-related reactions.
- Subsequent infusions: Administer infusion over 1 to 2 hours if prior infusions were tolerated. Observe patients during the infusion and for at least 30 minutes after infusion.
- Premedication: Prior to each dose of TRODELVY, premedication for prevention of infusion reactions and prevention of chemotherapy-induced nausea and vomiting (CINV) is recommended. Premedicate with antipyretics, H1 and H2 blockers prior to infusion, and corticosteroids may be used for patients who had prior infusion reactions. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK_1 receptor antagonist, as well as other drugs as indicated).

Dose Modifications for Infusion-related Reactions: Slow or interrupt the infusion rate of TRODELVY if the patient develops an infusion-related reaction. Permanently discontinue TRODELVY for life-threatening infusion-related reactions.

Dose Modifications for Adverse Reactions: Withhold or discontinue TRODELVY to manage adverse reactions as described below. Do not re-escalate the TRODELVY dose after a dose reduction for adverse reactions has been made.

Severe Neutropenia, defined as Grade 4 neutropenia ≥7 days, OR Grade 3 febrile neutropenia (absolute neutrophil count or ANC <1000/mm^3 and fever ≥38.5°C), OR at time of scheduled treatment, Grade 3-4 neutropenia which delays dosing by 2 or 3 weeks for recovery to ≤ Grade 1:

- At first occurrence, 25% dose reduction and administer granulocyte-colony stimulating factor (G-CSF). At second occurrence, 50% dose reduction. At third occurrence, discontinue TRODELVY.
- At time of scheduled treatment, if Grade 3-4 neutropenia occurs which delays dosing beyond 3 weeks for recovery to ≤Grade 1, discontinue TRODELVY at first occurrence.

Severe Non-Neutropenic Toxicity, defined as Grade 4 non-hematologic toxicity of any duration, OR any Grade 3-4 nausea, vomiting or diarrhea due to treatment that is not controlled with antiemetics and anti-diarrheal agents, OR other Grade 3-4 non-hematologic toxicity persisting >48 hours despite optimal medical management, OR at time of scheduled treatment, Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, which delays dose by 2 or 3 weeks for recovery to ≤Grade 1:

- At first occurrence, 25% dose reduction. At second occurrence, 50% dose reduction. At third occurrence, discontinue TRODELVY.
- In the event of Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, which does not recover to ≤Grade 1 within 3 weeks, discontinue TRODELVY at first occurrence.

CONTRAINDICATIONS

*Also see **Warnings and Precautions***

TRODELVY is contraindicated in patients who have experienced a severe hypersensitivity reaction to TRODELVY.

WARNINGS AND PRECAUTIONS

*Also see **BOXED WARNING, Dosage and Administration, Contraindications, Clinical Pharmacology, Nonclinical Toxicology,** and **Use in Specific Populations***

Neutropenia: Severe, life-threatening, or fatal neutropenia can occur in patients treated with TRODELVY. Neutropenia occurred in 61% of patients treated with TRODELVY. Grade 3-4 neutropenia occurred in 47% of patients. Febrile neutropenia occurred in 7% of patients. Withhold TRODELVY for ANC below 1500/mm^3 on Day 1 of any cycle or neutrophil count below 1000/mm^3 on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Dose modifications may be required due to neutropenia.

Diarrhea: TRODELVY can cause severe diarrhea. Diarrhea occurred in 65% of all patients treated with TRODELVY. Grade 3-4 diarrhea occurred in 12% of all patients treated with TRODELVY. One patient had intestinal perforation following diarrhea. Neutropenic colitis occurred in 0.5% of patients. Withhold TRODELVY for Grade 3-4 diarrhea at the time of scheduled treatment administration and resume when resolved to ≤ Grade 1. At the onset of diarrhea, evaluate for infectious causes and if negative, promptly initiate loperamide, 4 mg initially followed by 2 mg with every episode of diarrhea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures (e.g., fluid and electrolyte substitution) may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment with TRODELVY (e.g., abdominal cramping, diarrhea, salivation, etc.) can receive appropriate premedication (e.g., atropine) for subsequent treatments.

Hypersensitivity and Infusion-Related Reactions: Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY treatment. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 37% of patients treated with TRODELVY. Grade 3-4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.3%. The incidence of anaphylactic reactions was 0.3%. Premedication for infusion reactions in patients receiving TRODELVY is recommended. Have medications and emergency equipment to treat infusion-related reactions, including anaphylaxis, available for immediate use when administering TRODELVY. Closely monitor patients for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Permanently discontinue TRODELVY for Grade 4 infusion-related reactions.

Nausea and Vomiting: TRODELVY is emetogenic. Nausea occurred in 66% of all patients treated with TRODELVY. Grade 3 nausea occurred in 4% of patients. Vomiting occurred in 39% of patients. Grade 3-4 vomiting occurred in 3% of these patients. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK_1 receptor antagonist as well as other drugs as indicated) for prevention of CINV. Withhold TRODELVY doses for Grade 3 nausea or Grade 3-4 vomiting and resume with additional supportive measures when resolved to ≤Grade1. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting.

Increased Risk of Adverse Reactions in Patients with Reduced UGT1A1 Activity: Patients homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk for neutropenia, febrile neutropenia, and anemia and may be at increased risk for other adverse reactions with TRODELVY. The incidence of neutropenia and anemia was analyzed in 701 patients who received TRODELVY and had UGT1A1 genotype results. The incidence of Grade 3-4 neutropenia was 67% in patients homozygous for the UGT1A1*28 (n=87), 46% in patients heterozygous for the UGT1A1*28 allele (n=301), and 46% in patients homozygous for the wild-type allele (n=313). The incidence of Grade 3-4 anemia was 25% in patients homozygous for the UGT1A1*28 allele, 10% in patients heterozygous for the UGT1A1*28 allele, and 11% in patients homozygous for the wild-type allele. Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue TRODELVY based on onset, duration, and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced UGT1A1 enzyme activity.

Embryo-Fetal Toxicity: Based on its mechanism of action, TRODELVY can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. TRODELVY contains a genotoxic component, SN-38, and targets rapidly dividing cells. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose.

ADVERSE REACTIONS

*Also see **BOXED WARNING, Warnings and Precautions,** and **Clinical Studies***

The pooled safety population described in the Warnings and Precautions section reflect exposure to TRODELVY as a single agent in 795 patients from three studies, IMMU-132-01, IMMU-132-05 and IMMU-132-06 which included 366 patients with mTNBC who had received prior systemic chemotherapy for advanced disease and 180 patients with mUC. Among the 795 patients treated with TRODELVY, the median duration of treatment was 4.1 months (range: 0 to 59 months). The most common (≥ 25%) adverse reactions were nausea (66%), diarrhea (65%), fatigue (62%), neutropenia (61%), alopecia (45%), anemia (42%), vomiting (39%), constipation (37%), decreased appetite (34%), rash (32%) and abdominal pain (28%).

Metastatic Triple-Negative Breast Cancer

The safety of TRODELVY was evaluated in a randomized, active-controlled, open-label trial (ASCENT, IMMU-132-05) in patients with mTNBC who had previously received a taxane and at least two prior therapies. Patients were randomized (1:1) to receive either TRODELVY (n=258) or single agent chemotherapy (n=224) and were treated until disease progression or unacceptable toxicity. For patients treated with TRODELVY, the median duration of treatment was 4.4 months (range: 0 to 23 months). Serious adverse reactions occurred in 27% of patients, and those in > 1% included neutropenia (7%), diarrhea (4%), and pneumonia (3%). Fatal adverse reactions occurred in 1.2% of patients, including respiratory failure (0.8%) and pneumonia (0.4%). TRODELVY was permanently discontinued for adverse reactions in 5% of patients. These adverse reactions (≥1%) were pneumonia (1%) and fatigue (1%). The most frequent (≥5%) adverse reactions leading to a treatment interruption in 63% of patients were neutropenia (47%), diarrhea (5%), respiratory infection (5%), and leukopenia (5%). The most frequent (>4%) adverse reactions leading to a dose reduction in 22% of patients were neutropenia (11%) and diarrhea (5%). G-CSF was used in 44% of patients who received TRODELVY. The most common adverse reactions (≥25%) were fatigue, neutropenia, diarrhea, nausea, alopecia, anemia, constipation, vomiting, abdominal pain, and decreased appetite. The most common Grade 3-4 lab abnormalities (≥25%) were decreased neutrophils (49%), decreased leukocytes (41%), and decreased lymphocytes (31%).

Locally Advanced or Metastatic Urothelial Cancer

The safety of TRODELVY was evaluated in a single-arm, open-label study (TROPHY, IMMU-132-06) in patients (n=113) with mUC who had received previous platinum-based and anti-PD-1/PD-L1 therapy. Serious adverse reactions occurred in 44% of patients, and those in >1% included infection (18%), neutropenia (12%, including febrile neutropenia in 10%), acute kidney injury (6%), urinary tract infection (6%), sepsis or bacteremia (5%), diarrhea (4%), anemia, venous thromboembolism, and small intestinal obstruction (3% each), pneumonia, abdominal pain, pyrexia, and thrombocytopenia (2% each). Fatal adverse reactions occurred in 3.6% of patients, including sepsis, respiratory failure, epistaxis, and completed suicide. TRODELVY was permanently discontinued for adverse reactions in 10% of patients. The most frequent of these adverse reactions was neutropenia (4%, including febrile neutropenia in 2%). The most common adverse reactions leading to dose interruption in 52% of patients were neutropenia (27%, including febrile neutropenia in 2%), infection (12%), and acute kidney injury (8%). The most common (>4%) adverse reactions leading to a dose reduction in 42% of patients were neutropenia (13%, including febrile neutropenia in 3%), diarrhea (11%), fatigue (8%), and infection (4%). G-CSF was used in 47% of patients who received TRODELVY. The most common adverse reactions (incidence ≥25%) were diarrhea, fatigue, neutropenia, nausea, any infection, alopecia, anemia, decreased appetite, constipation, vomiting, rash, and abdominal pain. The most common Grade 3-4 lab abnormalities (≥25%) were decreased neutrophils (43%), decreased leukocytes (38%), and decreased lymphocytes (35%). Other clinically significant adverse reactions (≤15%) include: peripheral neuropathy (12%), sepsis or bacteremia (9%), and pneumonia (4%).

DRUG INTERACTIONS

*Also see **Warnings and Precautions** and **Clinical Pharmacology***

UGT1A1 Inhibitors: Concomitant administration of TRODELVY with inhibitors of UGT1A1 may increase the incidence of adverse reactions due to potential increase in systemic exposure to SN-38. Avoid administering UGT1A1 inhibitors with TRODELVY.

UGT1A1 Inducers: Exposure to SN-38 may be substantially reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY.

USE IN SPECIFIC POPULATIONS:

*Also see **Warnings and Precautions, Clinical Pharmacology,** and **Nonclinical Toxicology***

Pregnancy: TRODELVY can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. There are no available data in pregnant women to inform the drug-associated risk. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

Lactation: There is no information regarding the presence of sacituzumab govitecan-hziy or SN-38 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 women not to breastfeed during treatment and for 1 month after the last dose of TRODELVY.

Females and Males of Reproductive Potential: Verify the pregnancy status of females of reproductive potential prior to initiation. TRODELVY can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose.

Males: Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose.

Infertility: Based on findings in animals, TRODELVY may impair fertility in females of reproductive potential.

Pediatric Use: Safety and effectiveness of TRODELVY have not been established in pediatric patients.

Geriatric Use: Of the patients who received TRODELVY, 264/795 (33%) of all patients were ≥ 65 years old, and 11% were ≥75 years old. No overall differences in safety and effectiveness were observed between these patients and younger patients.

Hepatic Impairment: No adjustment to the starting dose is required when administering TRODELVY to patients with mild hepatic impairment (bilirubin ≤ 1.5 ULN and AST/ALT < 3 ULN). The safety of TRODELVY in patients with moderate or severe hepatic impairment has not been established, and no recommendations can be made for the starting dose in these patients.

See PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

GILEAD

TRODELVY™
sacituzumab govitecan-hziy
180 mg for injection

1 in 8 cancer patients has a hereditary genetic variant[1]

Imagine knowing more. INVITAE

Reference: 1. Samadder NJ, Riegert-Johnson D, Boardman L, et al. Comparison of universal genetic testing vs guideline-directed targeted testing for patients with hereditary cancer syndrome. *JAMA Oncol.* 2021;7(2):230-237. doi:10.1001/jamaoncol.2020.6252.

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SPOTLIGHTS

DEPARTMENTS

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

Email to FCSCommunications@FLCancer.com

On the cover: FCS patient Tarralyn Jones. Photo courtesy of Griffith Photography.

FCS THE MAGAZINE

NATHAN H. WALCKER, CHIEF EXECUTIVE OFFICER:

Everything we do at FCS is centered on the patients who entrust us with their care.

As we enter the final quarter of this year, I could not be more pleased with what we have been able to accomplish amidst the nonstop challenges of the continuing pandemic and the ever-evolving oncology care landscape. I took a bit of time recently, as I concluded my first full year as CEO, to reflect on the progress we have made and invite you to read the full article on page 10.

A recent significant development is the opening of our third Drug Development Unit in Lake Nona. Partnering with the Sarah Cannon Research Institute, FCS is part of a network reaching more clinical trial patients than any single cancer center. Dr. Gus Fonseca, Medical Director of the Clinical Research Program, shares how important discoveries will advance more rapidly through this exciting expansion in Central Florida.

It is rare that a community oncology provider is able to offer patients the depth and range of the most advanced and promising cancer treatments — and to do it with such focus and compassion.

I am grateful to all of our FCS physicians and team members for your outstanding efforts.

LUCIO GORDAN, MD, PRESIDENT & MANAGING PHYSICIAN:

Each day, the work we do is helping to expand clinical knowledge and, most importantly, enhancing the quality of life for our patients. Our cover story is proof of that. Tarralyn Jones, a patient cared for by Dr. David Molthrop and our team in Winter Park, is able to call herself a three-time cancer survivor, and she shares her inspiring story with great enthusiasm.

Cancer patients cannot have hope without access to care, and that is why our advocacy efforts at the local, statewide and national levels are so integral to our success.

We are proud to have joined with our colleagues across the country to sponsor a national campaign designed to reverse the troubling pandemic trend of Americans delaying critical cancer screenings, resulting in later stage diagnosis for many.

As partners with the Community Oncology Alliance Patient Advocacy Network, known as CPAN, we are engaging patients in sharing their stories with elected officials so that they more clearly understand the value of community oncology and the issues that affect quality and availability.

Our Advocacy Update includes more details on these vital activities. We remain committed to expanding partnerships that enable us to enhance the care we provide to our communities.

Thank you all for your support.

PATIENT FEATURE

‘It’s All About Your Mindset!’

Cancer survivor Tarralyn Jones shares life lessons

BY KARI C. BARLOW

Kindness. Compassion. Sincerity.

Those are the words that come to mind when Tarralyn Jones thinks about Florida Cancer Specialists & Research Institute (FCS).

And as a three-time cancer survivor who has spent more than her fair share of time at the FCS Winter Park clinic, she has earned the right to have an opinion.

“Every time I go, I am greeted and called by name,” said Tarralyn, a motivational speaker and the founder of TJ’s Designs and Events in Winter Park. “They know who you are, and that’s just excellent customer service. It’s like a family atmosphere.”

Tarralyn first found her way to FCS in 2002 after a mammogram revealed a complex mass in her right breast. Under the care of Dr. David Molthrop, she endured eight aggressive chemotherapy treatments, ultimately reaching a good outcome.

“Dr. Molthrop truly cares about his patients,” she said. “It isn’t scripted. He truly cares, and there is a level of trust there.”

In the years that followed, Tarralyn and her family — husband Willie and their three children, Brian, Candace and Christian — would find out just how much that trust mattered.

In 2008, her breast cancer returned, and it wasn’t easy.

“You’re dealing with the treatment, the hair loss and nausea and you’re looking at your kids’ faces, and they’re wondering if you’re going to be here,” Tarralyn said.

But once again, she sought treatment, fought hard and moved on with her life.

In 2014, on a frightening day Tarralyn still recalls vividly, she felt a little off while driving around town.

“I had a throbbing headache, and I could not see,” she said. “To this day I can’t tell you how I got home. … By the time I did arrive, I couldn’t see how to put the car in park. The pain was excruciating.”

Dr. David Molthrop, MD

The breast cancer had metastasized to her brain, and she immediately underwent surgery to remove two tumors.

Seven years later, Tarralyn still has regular follow-up appointments with Dr. Molthrop, who is in awe of her resilience and resolve to keep fighting.

"The hardest part for us, as physicians, is recurrence," said Dr. Molthrop, who has worked as an oncologist for almost 30 years. "A lot of times the patients have fought it and gone on with their lives, and that's one of the most difficult conversations to have.

"Tarralyn is an easy person to talk to. She steels herself for those conversations, and that actually makes it easier for us, which is certainly not the goal."

Dr. Molthrop said his focus is always on helping patients process the information he is delivering, whether it's a first-time diagnosis or the news of recurring cancer.

"The thing I think is most important is taking what can be a complicated and emotionally exhausting subject and making it understandable for the patient," he said.

"He listens very closely to find out what side effects I'm having. That means a lot. When you have sincerity, care and compassion, it makes a difference and helps you focus on getting better."

For Tarralyn, having Dr. Molthrop's full support and guidance over the past 12 years has been a vital piece of her recovery.

"He looks at all the alternatives. He takes the time to research," she said. "He listens very closely to find out what side effects I'm having. That means a lot. When you have sincerity, care and compassion, it makes a difference and helps you focus on getting better."

That commitment to her own health and well-being is something that emerged after Tarralyn's first cancer diagnosis. Before cancer, she was busy pouring her energy into her family.

"We as women wear many hats in our homes," she recalls. "And I was neglecting myself."

Surviving three bouts of cancer opened her eyes to the necessity of self-care.

"Now I prioritize myself. My appointments, my follow-ups — I'm first," says Tarralyn, who urges women to find their own "self-care diva" deep inside. "I don't take life for granted. I live life to the fullest because of cancer."

That includes her role as the National Events Coordinator for PFPMA, the Professional Football Players Mothers Association. Her son Christian plays for the NFL's Chicago Bears after a standout career at Florida State University.

Battling cancer, while scary and exhausting, has brought clarity. She now places a high priority on not only her own health but also the health of those around her and nurturing the relationships that help you weather the hard times.

"Let's be real, sometimes you need someone to hold your shoulders up!"

When Tarralyn needed support, she relied on her faith and a strong prayer life, her family and her trusted friends. She also dug deep within herself and found the will to move forward.

"I do have a stubborn nature," she says with a laugh. "I'm not going to buy into being defeated. And it's all about your mindset."

As Tarralyn looks to the future, her mission is to encourage women to put their health first and live every day like the blessing it is.

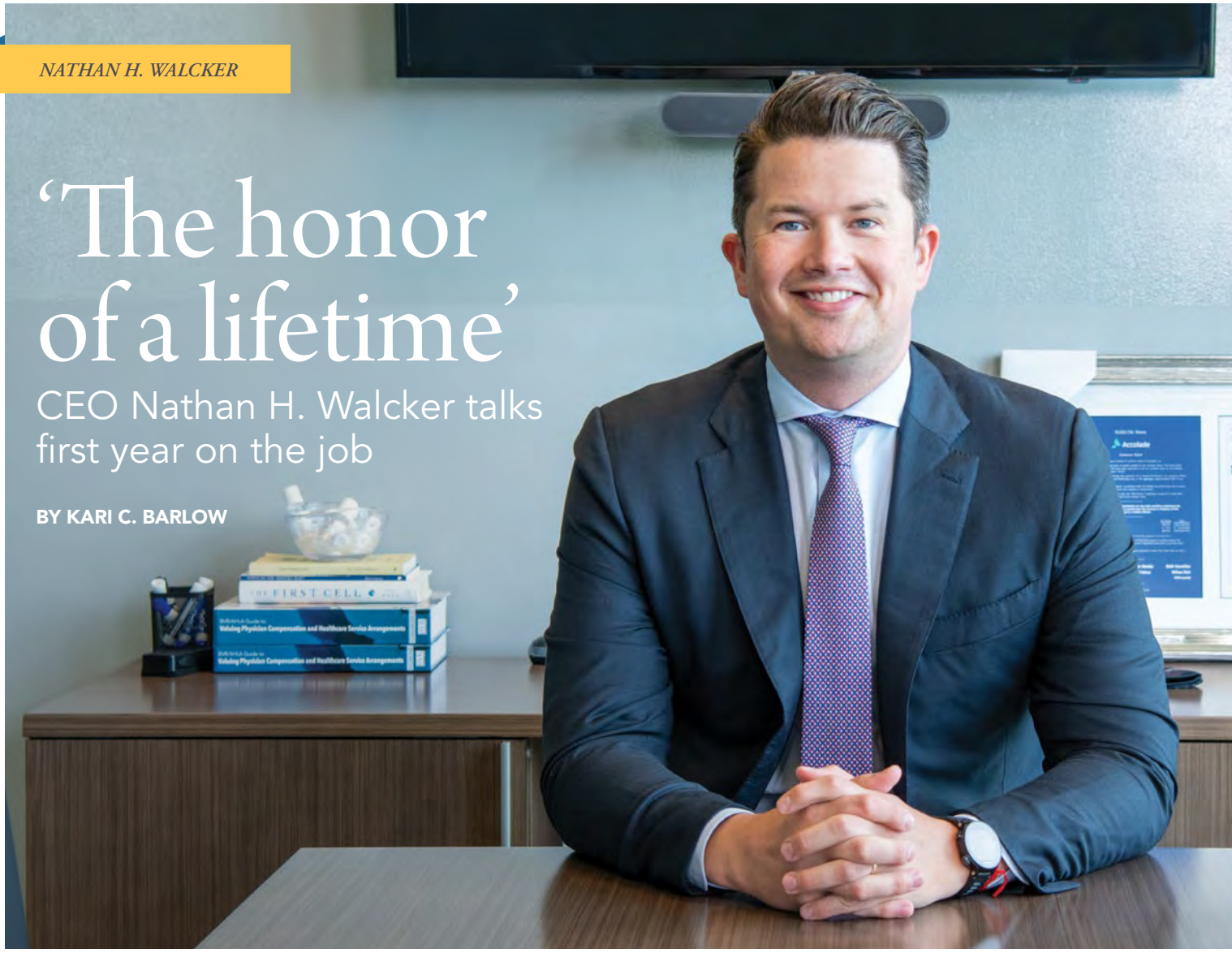
"For women who say they're too busy, take the time to concentrate on your health by making your appointments, keeping them and being diligent in follow-up appointments," she says. "And remember that early detection is key and can save your life."

NATHAN H. WALCKER

'The honor of a lifetime'

CEO Nathan H. Walcker talks first year on the job

BY KARI C. BARLOW



When Nate Walcker reflects on his first year as CEO of Florida Cancer Specialists & Research Institute (FCS), he primarily feels a profound sense of gratitude.

Walcker, who originally joined FCS in 2019 as Chief Financial Officer, took the helm on Aug. 1, 2020, just five months into the global pandemic.

"It was exhilarating. It was scary. It was emotional at times and challenging, but in a constructive way," he recalled. "Those early days forced me to adapt and be flexible to confront the present-day reality of leading FCS amidst COVID-19, versus rolling out our first 100-day strategy and communicating the broader vision for FCS."

Looking back, Walcker is quick to attribute any success he's had to the skill, dedication and resolve of the FCS workforce.

"It was the relentless effort of my 4,200 teammates across FCS who really gave their all," he said. "It's truly taken a village."

Since early 2020, FCS has faced its share of COVID-19-related obstacles, from procurement shortages to staffing issues to the challenge of protecting its vulnerable patients from the spread of the virus. While FCS clinics managed to remain open, the Company had to send home hundreds of employees to work remotely. In a short span of time, teammates in all divisions at all levels were forced to dig in and get creative.

"I couldn't be prouder of our team — for showing up, for being flexible and being able to execute in a fluid, uncertain environment," Walcker said. "It took all of us rowing the boat in the same direction to deliver for our patients."

And he points out that FCS hasn't simply survived the past 12 to 18 months — it's thrived.

In March 2020, the practice opened its new Lake Mary Cancer Center and Sarah Cannon Research Institute Drug Development Unit, a 25,000-square-foot facility that combines medical oncology and hematology services and phase one clinical trial research under one roof. FCS has launched new cancer centers in The Villages, Tallahassee, Delray Beach, Sebring, Estero, Jacksonville and on the University of Central Florida Cancer Center Campus in Orlando.

"I have the tremendous privilege of sitting in this seat ... and every day I wake up, I need to continue to earn it."

In October 2020, FCS opened a new oncolytic specialty pharmacy facility in Fort Myers and, since then, has broken ground on several new cancer centers in a variety of locations that include Bradenton, Altamonte Springs, Clermont and Orange City.

Walcker is especially proud of the FCS genetics lab expanding to provide in-house molecular testing, or next generation sequencing (NGS), for its patients. In July of this year, the lab began offering testing to assist in the diagnosis, prognosis and treatment planning of a wide variety of cancers, including solid tumors and hematological malignancies.

"Bringing next generation sequencing to FCS is an incredible leap forward for community oncology," he said. "It allows us to identify mutations in hundreds of genes, and really understand each patient's unique diagnosis. We're bringing precision medicine into the community. Our lab infrastructure and talent have perfectly positioned FCS to be a leader in the field."

These strategic investments — along with FCS' ongoing commitment to early phase drug development and research— are all part of Walcker's determination to lead from the front.

"It goes back to us delivering on our mission to be at the forefront of oncology treatment not just across Florida, but nationally," he said. "Research can't just be in our name. We have to live and breathe it every day."

While Walcker sees major growth in FCS' future, he plans to take a balanced approach that aligns with his top three priorities: 1) placing patients at the center of everything FCS does, 2) being a progressive, sought-after employer, and 3) providing FCS physicians and researchers with the technology, talent and resources necessary to break new ground.

"If we do that, everything will fall into place and good things will come," he said. "FCS is already a leader in cancer treatment … a preeminent brand. Going forward, what we need to be doing is making sure we are a destination for cancer care."

That includes, according to Walcker, maintaining a sharp focus on being the gold standard for value-based oncology care.

Since taking over as CEO, Walcker has often been reminded of a well-known quote by tennis icon Billie Jean King: "Pressure is a privilege."

"I have the tremendous privilege of sitting in this seat," he shared. "And every day I wake up, I need to continue to earn it."

A former Wall Street investment banker, Walcker was drawn to FCS because of a desire to make a lasting impact on people's lives and the chance to be part of a company that is solely focused on taking care of cancer patients. What he's witnessed in the past year has been nothing short of life changing.

"It has fundamentally shifted my appreciation of what FCS does for its patients," he said. "It's incredibly complex. Our physicians, our nurse practitioners, our teams who show up every day — these folks are rock stars in my book."

Walcker said he's proud to be part of the Company that gives thousands of people across Florida access to a best-in-class provider for cancer care.

"My role at FCS truly is an honor of a lifetime," he said. "I could not be more enthused about what the next year holds and what we are doing to make sure that community oncology remains a viable choice for patients well into the future."

LAKE NONA DDU

Lake Nona Drug Development Unit Expands Access to Clinical Trials

BY TIM LINAFELT

With the opening of the new, state-of-the-art Sarah Cannon Drug Development Unit in Lake Nona, Florida Cancer Specialists & Research Institute (FCS) is part of something that, at first blush, sounds like it should be impossible: It's made the world both bigger and smaller.

Bigger because it has opened an entirely new world of trials, treatments and care that not so long ago were hard to find and even harder to reach. Smaller because these treatments are now just down the road for the millions of people residing in Central Florida — and no more than a few hours from anywhere in the state.

In collaboration with the University of Central Florida (UCF) College of Medicine, the Sarah Cannon DDU focuses exclusively on oncology clinical trials at the earliest phases of research and was designed to meet the specialized needs of patients seeking advanced cancer treatment options.

The first patient was treated on a clinical trial at the new unit in September. The 10,000-square-foot, free-standing facility, located in the Sarah Cannon | UCF Lake Nona Cancer Center campus, is in the same location as the FCS Lake Nona clinic, which opened in February and has already made a big first impression.

"It's much closer, much faster, yet it comes with the same rigor of the scientific process," said Gustavo Fonseca, MD, FACP, Medical Director of the FCS Clinical Research Program. "We know patients are going to be treated well, but now they don't have to go to a much more distant and difficult-to-reach tertiary care center."

The first benefit of the Lake Nona DDU is apparent as soon as a visitor looks out the front door. The UCF Lake Nona Medical Center is mere feet away, and the Orlando VA Medical Center is not much further.

For many patients, access to their hospitals — including their trusted doctors, nurses, specialists and now, novel treatments — will all be in one centralized location.

That sure beats the stress of road trips, airports and hotels.

"There is more available that is closer to home," said FCS Director of Clinical Research Bucky Jones-Lombard. "Which is what the whole focus of FCS is — bringing care to the patient, rather than the patient having to come to the care."

More than that, though, patients who visit the Lake Nona DDU will have the opportunity to experience the potentially lifesaving benefits offered from clinical trials and research.

Specifically, the facility will offer qualifying patients the chance to participate in Phase I trials. That, both Dr. Fonseca and Jones-Lombard said, is what really sets the Lake Nona DDU apart.

"It's a great setting for Sarah Cannon's early-phase research program," Jones-Lombard said.

Fonseca, who joined FCS in 2013 and was appointed to his current post earlier this year, recalled a time when patients who wanted to participate in such trials were forced to travel to all corners of the country — often New York, Boston or Houston.

And once they got to those faraway places, they might often find themselves in a fierce competition for time and attention.

"Those were almost the only sites in the whole country that were getting to try new drugs and new opportunities for patients," Fonseca said. "So you'd have to get on an airplane.

"Now, you can have the same access to the same medications at the same time."

Fonseca is particularly excited about the potential for advancement in targeted therapies — drugs that are tuned to address specific cancer molecules, which might provide a more tailored and effective course of action.

"Instead of the old days where we used to say, 'OK, you've got lung cancer. We've got three (chemotherapies), we're going to choose two and give them to you,' now we are a lot more specific," Fonseca said.

"We diagnose, then we figure out what

mutation a patient may have, and then, depending on what mutation they have, we give them the specific drugs. Through our partnership with Sarah Cannon, we've had those exact clinical trials here in Florida. And all of these are compounds that, three years ago, didn't exist."

Still, beyond all the trials and treatments and medical advances to come, Fonseca is most proud of what the Lake Nona DDU represents — FCS' steadfast commitment to patients and their families.

"We at FCS are ready to take that responsibility that is entrusted to us by the patients and their families and make sure that they're taken care of with the utmost technical and medical know-how in order to make their circumstances the most successful possible," he said.

Meet Cesar Augusto Perez, MD

The Lake Nona DDU is led by Cesar Augusto Perez, MD, a recognized expert in Phase 1 oncology research who has dedicated his career to translational oncology. Dr. Perez most recently served as an Associate Professor of Medicine at the University of Miami where he also was one of the leaders for Phase 1 oncology clinical research. He was previously an Assistant Professor of Medicine at the University of Louisville, where he received the Best Faculty Teacher Award in 2015 and 2017. After completing a hematology and oncology fellowship at the University of Miami, Dr. Perez received the Peter A. Cassileth, MD Award as an outstanding fellow, and served as Chief Fellow.

Dr. Perez works with a team that includes Sarah Canon and FCS research nurses, pharmacists and patient-support members who provide patients with access to the latest research and compassionate care without needing to travel far from home.


Patti LaBelle

Hey Florida: *It's Time to Screen for Cancer!*

BY LUCIO GORDAN, MD
FCS PRESIDENT & MANAGING PHYSICIAN


Lucio Gordan, MD

The COVID-19 pandemic understandably caused many people to skip important cancer screenings because they were worried about their safety. In fact, while breast, colon, prostate and lung cancers did not stop for COVID-19 in 2020, screenings and treatments did — dramatically.

A study that I co-authored and was published in the journal JCO Clinical Cancer Informatics, showed a considerable drop in cancer screening, diagnosis and treatment for American seniors and Medicare beneficiaries in 2020.

The study, which was conducted for the nonprofit Community Oncology Alliance by Avalere Health, examined common cancer procedures, including screenings and infusion therapies, such as chemotherapy, surgeries and radiation therapy. It found significant reductions in breast (down 85%), colon (-75%), prostate (-74%) and lung cancer (-56%) screenings at the first peak of the pandemic in April 2020, compared with April 2019. Our fellow oncologists say they are already starting to see the traumatic results as cancers are caught at later stages requiring more complex treatments, resulting in higher morbidity, or worse, death.

"I've learned timing is everything in life, and right now, it's time to take control of your health. I know what it's like to lose loved ones far too early to cancer. Don't wait until it's too late. I tell everyone, 'Honey, it's time to get screened.' "
– Patti LaBelle

In the early days of the pandemic, shelter-in-place orders and patient concerns about COVID-19 caused a massive drop in common, preventative screenings, such as mammograms and colonoscopies, as well as the cancer therapies and surgical procedures that occur as a result. While this reduction in services was expected as lockdowns took place, several cancer care providers have reported first-hand that they have not seen the complete resumption of services — and that it will take some time for a year of lost screenings to be made up.

Thankfully, medical centers, doctors' offices and screening facilities are now open, and staff are working hard to keep patients protected so that people can get screened for cancer in safe and convenient environments. Now it's important for people to maintain control of their health and connect with a local clinician to schedule recommended cancer screenings.
It's Time to Screen.

Early detection and diagnosis for common cancers may allow for less extensive treatment, with fewer side effects and long-term health issues, and it may even save lives. Unfortunately, cancer is the second leading cause of death in the United States, and Florida has the second highest cancer burden in the nation. Black adults have higher death rates than all other racial/ethnic groups for many cancer types. Cancer is the leading cause of death for Hispanic and Latino adults. Social determinants of health including incomes, health literacy and physical access to care contribute to these disparities.

Early cancer detection may save lives. As we emerge from the pandemic, it's time for Floridians to schedule their regular cancer screenings like mammograms and colonoscopies.

Patients, caregivers and friends of the FCS community who have questions about screenings can visit Time to Screen, a new FREE resource that helps connect people to convenient screening locations. We are committed to safeguarding your health and well-being, which is why we are excited to support this effort with CancerCare and the Community Oncology Alliance — two trusted national nonprofits leading this campaign.

The campaign has also partnered with two-time Grammy award winner and "Godmother of Soul" Patti LaBelle to help spread the word. LaBelle is appearing in television, digital and radio public service announcements as part of the nationwide effort to remind adults, especially those over the age of 40, to schedule doctor recommended regular screenings for six common cancers: breast, colorectal, cervical, prostate, lung and skin.

"I've learned timing is everything in life, and right now, it's time to take control of your health," said LaBelle. "I know what it's like to lose loved ones far too early to cancer. Don't wait until it's too late. I tell everyone, 'Honey, it's time to get screened.' "

Now is the time to resume cancer screenings. You or your loved ones can call (855) 53-SCREEN or visit TimetoScreen.org to learn about the benefits of screening and to find a convenient screening location.

Florida, it's time to screen!

Not an actual patient

GILOTRIF IS THE *ONLY* ORAL, CHEMO-FREE AGENT APPROVED FOR METASTATIC SQUAMOUS NSCLC

PROGRESSING AFTER PLATINUM-BASED CHEMOTHERAPY, REGARDLESS OF MUTATION STATUS[1,2]

Visit **www.gilotrifhcp.com/squamous-mnsclc** to learn more

Consider GILOTRIF as early as second-line for patients with metastatic squamous NSCLC who progressed after platinum-based chemotherapy[1,2]

INDICATIONS AND USAGE

- **GILOTRIF is indicated for** the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy.

IMPORTANT SAFETY INFORMATION FOR GILOTRIF® (afatinib) TABLETS

WARNINGS AND PRECAUTIONS

Diarrhea

- GILOTRIF can cause diarrhea which may be severe and can result in dehydration with or without renal impairment. In clinical studies, some of these cases were fatal.
- For patients who develop Grade 2 diarrhea lasting more than 48 hours or Grade 3 or greater diarrhea, withhold GILOTRIF until diarrhea resolves to Grade 1 or less, and then resume at a reduced dose.
- Provide patients with an anti-diarrheal agent (e.g., loperamide) for self-administration at the onset of diarrhea and instruct patients to continue anti-diarrheal until loose stools cease for 12 hours.

Bullous and Exfoliative Skin Disorders

- GILOTRIF can result in cutaneous reactions consisting of rash, erythema, and acneiform rash. In addition, palmar-plantar erythrodysesthesia syndrome was observed in clinical trials in patients taking GILOTRIF.
- Discontinue GILOTRIF in patients who develop life-threatening bullous, blistering, or exfoliating skin lesions. For patients who develop Grade 2 cutaneous adverse reactions lasting more than 7 days, intolerable Grade 2, or Grade 3 cutaneous reactions, withhold GILOTRIF. When the adverse reaction resolves to Grade 1 or less, resume GILOTRIF with appropriate dose reduction.
- Postmarketing cases of toxic epidermal necrolysis (TEN) and Stevens Johnson syndrome (SJS) have been reported in patients receiving GILOTRIF. Discontinue GILOTRIF if TEN or SJS is suspected.

Interstitial Lung Disease

- Interstitial Lung Disease (ILD) or ILD-like adverse reactions (e.g., lung infiltration, pneumonitis, acute respiratory distress syndrome, or alveolitis allergic) occurred in patients receiving GILOTRIF in clinical trials. In some cases, ILD was fatal. The incidence of ILD appeared to be higher in Asian patients as compared to white patients.
- Withhold GILOTRIF during evaluation of patients with suspected ILD, and discontinue GILOTRIF in patients with confirmed ILD.

Hepatic Toxicity

- Hepatic toxicity as evidenced by liver function tests abnormalities has been observed in patients taking GILOTRIF. In 4257 patients who received GILOTRIF across clinical trials, 9.7% had liver test abnormalities, of which 0.2% were fatal.
- Obtain periodic liver testing in patients during treatment with GILOTRIF. Withhold GILOTRIF in patients who develop worsening of liver function. Discontinue treatment in patients who develop severe hepatic impairment while taking GILOTRIF.

Gastrointestinal Perforation

- Gastrointestinal (GI) perforation, including fatal cases, has occurred with GILOTRIF. GI perforation has been reported in 0.2% of patients treated with GILOTRIF among 3213 patients across 17 randomized controlled clinical trials.
- Patients receiving concomitant corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), or anti-angiogenic agents, or patients with increasing age or who have an underlying history of GI ulceration, underlying diverticular disease, or bowel metastases may be at an increased risk of perforation.
- Permanently discontinue GILOTRIF in patients who develop GI perforation.

Please see additional Important Safety Information and Brief Summary of Prescribing Information on the following pages.

GILOTRIF® (afatinib) tablets

Recommended dose[1]

- The recommended dose is 40 mg orally once daily
- In patients with pre-existing severe renal impairment, the recommended dose of GILOTRIF is 30 mg orally once daily*

How to take[1]

- Take GILOTRIF at least 1 hour before or 2 hours after a meal
- Do not take a missed dose within 12 hours of the next dose

Treatment duration[1]

- Treatment should be continued until disease progression or until no longer tolerated by the patient

Multiple strengths[1]

- Multiple tablet strengths are available for dose adjustment: 40 mg, 30 mg, and 20 mg

*Estimated glomerular filtration rate (eGFR) 15 to 29 mL/min/1.73 m^2.

WARNINGS AND PRECAUTIONS (cont'd)

Keratitis

- Keratitis has been reported in patients taking GILOTRIF.
- Withhold GILOTRIF during evaluation of patients with suspected keratitis. If diagnosis of ulcerative keratitis is confirmed, interrupt or discontinue GILOTRIF. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered. GILOTRIF should be used with caution in patients with a history of keratitis, ulcerative keratitis, or severe dry eye. Contact lens use is also a risk factor for keratitis and ulceration.

Embryo-Fetal Toxicity

- GILOTRIF can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.
- Advise females of reproductive potential to use effective contraception during treatment, and for at least 2 weeks after the last dose of GILOTRIF. Advise female patients to contact their healthcare provider with a known or suspected pregnancy.

ADVERSE REACTIONS

Adverse Reactions observed in clinical trials were as follows:

Previously Treated, Metastatic Squamous NSCLC

- In GILOTRIF-treated patients (n=392) the most common adverse reactions (≥20% all grades & vs erlotinib-treated patients (n=395)) were diarrhea (75% vs 41%), rash/acneiform dermatitis (70% vs 70%), stomatitis (30% vs 11%), decreased appetite (25% vs 26%), and nausea (21% vs 16%).
- Serious adverse reactions were reported in 44% of patients treated with GILOTRIF. The most frequent serious adverse reactions reported in patients treated with GILOTRIF were pneumonia (6.6%), diarrhea (4.6%), and dehydration and dyspnea (3.1% each). Fatal adverse reactions in GILOTRIF-treated patients included ILD (0.5%), pneumonia (0.3%), respiratory failure (0.3%), acute renal failure (0.3%), and general physical health deterioration (0.3%).

DRUG INTERACTIONS

Effect of P-glycoprotein (P-gp) Inhibitors and Inducers

- Concomitant use of P-gp inhibitors (including but not limited to ritonavir, cyclosporine A, ketoconazole, itraconazole, erythromycin, verapamil, quinidine, tacrolimus, nelfinavir, saquinavir, and amiodarone) with GILOTRIF can increase exposure to afatinib.
- Concomitant use of P-gp inducers (including but not limited to rifampicin, carbamazepine, phenytoin, phenobarbital, and St. John's wort) with GILOTRIF can decrease exposure to afatinib.

USE IN SPECIFIC POPULATIONS

Lactation

- Because of the potential for serious adverse reactions in breastfed infants from GILOTRIF, advise women not to breastfeed during treatment with GILOTRIF and for 2 weeks after the final dose.

Females and Males of Reproductive Potential

- GILOTRIF may reduce fertility in females and males of reproductive potential. It is not known if the effects on fertility are reversible.

Renal Impairment

- Patients with severe renal impairment (estimated glomerular filtration rate [eGFR] 15 to 29 mL/min/1.73 m^2) have a higher exposure to afatinib than patients with normal renal function. Administer GILOTRIF at a starting dose of 30 mg once daily in patients with severe renal impairment. GILOTRIF has not been studied in patients with eGFR <15 mL/min/1.73 m^2 or who are on dialysis.

Hepatic Impairment

- GILOTRIF has not been studied in patients with severe (Child Pugh C) hepatic impairment. Closely monitor patients with severe hepatic impairment and adjust GILOTRIF dose if not tolerated.

GF PROF ISI 10.21.19

References: 1. GILOTRIF [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc. **2.** Soria JC, Felip E, Cobo M, et al. Afatinib versus erlotinib as second-line treatment of patients with advanced squamous cell carcinoma of the lung (LUX-Lung 8): an open-label randomised controlled phase 3 trial. *Lancet Oncol.* 2015;16(8):897-907.

Please see Brief Summary of Prescribing Information on the following pages.

Boehringer Ingelheim

GILOTRIF® (afatinib) tablets, for oral use

Initial U.S. Approval: 2013

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Please see package insert for full Prescribing Information.

INDICATIONS AND USAGE: EGFR Mutation-Positive, Metastatic Non-Small Cell Lung Cancer: GILOTRIF is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test. Limitation of Use: The safety and efficacy of GILOTRIF have not been established in patients whose tumors have resistant EGFR mutations. **Previously Treated, Metastatic Squamous NSCLC:** GILOTRIF is indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy.

CONTRAINDICATIONS: None

WARNINGS AND PRECAUTIONS: Diarrhea: Diarrhea has resulted in dehydration with or without renal impairment across the clinical experience; some cases were fatal. Grade 3-4 diarrhea occurred in 697 (16%) of the 4257 patients who received GILOTRIF across 44 clinical trials. In LUX-Lung 3, diarrhea occurred in 96% of patients treated with GILOTRIF (n=229), of which 15% were Grade 3 in severity and occurred within the first 6 weeks. Renal impairment as a consequence of diarrhea occurred in 6% of patients treated with GILOTRIF, of which 1.3% were Grade 3. In LUX-Lung 8, diarrhea occurred in 75% of patients treated with GILOTRIF (n=392), of which 10% were Grade 3 in severity and 0.8% were Grade 4 in severity. Renal impairment as a consequence of diarrhea occurred in 7% of patients treated with GILOTRIF, of which 2% were Grade 3 *[see Adverse Reactions]*. For patients who develop prolonged Grade 2 diarrhea lasting more than 48 hours, or greater than or equal to Grade 3 diarrhea, withhold GILOTRIF until diarrhea resolves to Grade 1 or less, and resume GILOTRIF with appropriate dose reduction. Provide patients with an anti-diarrheal agent (e.g., loperamide) for self-administration at the onset of diarrhea and instruct patients to continue anti-diarrheal therapy until loose bowel movements cease for 12 hours. **Bullous and Exfoliative Skin Disorders:** Grade 3 cutaneous reactions characterized by bullous, blistering, and exfoliating lesions, occurred in 0.2% of the 4257 patients who received GILOTRIF across clinical trials. In LUX-Lung 3, the overall incidence of cutaneous reactions consisting of rash, erythema, and acneiform rash was 90%, and the incidence of Grade 3 cutaneous reactions was 16%. In addition, the incidence of Grade 1-3 palmar-plantar erythrodysesthesia syndrome was 7%. In LUX-Lung 8, the overall incidence of cutaneous reactions consisting of rash, erythema, and acneiform rash was 70%, and the incidence of Grade 3 cutaneous reactions was 7%. In addition, the incidence of Grade 1-3 palmar-plantar erythrodysesthesia syndrome was 1.5% *[see Adverse Reactions]*. Discontinue GILOTRIF in patients who develop life-threatening bullous, blistering, or exfoliating lesions. For patients who develop prolonged Grade 2 cutaneous adverse reactions lasting more than 7 days, intolerable Grade 2, or Grade 3 cutaneous reactions, withhold GILOTRIF until the adverse reaction resolves to Grade 1 or less, and resume GILOTRIF with appropriate dose reduction. Postmarketing cases consistent with toxic epidermal necrolysis (TEN) and Stevens Johnson syndrome (SJS) have been reported in patients receiving GILOTRIF. The cases of TEN and SJS bullous skin reactions result from a distinct and separate mechanism of toxicity than the bullous skin lesions secondary to the pharmacologic action of the drug on the epidermal growth factor receptor. Discontinue GILOTRIF if TEN or SJS is suspected. **Interstitial Lung Disease (ILD):** Interstitial lung disease or ILD-like adverse reactions (e.g., lung infiltration, pneumonitis, acute respiratory distress syndrome, or alveolitis allergic) occurred in 1.6% of the 4257 patients who received GILOTRIF across clinical trials; of these, 0.4% were fatal. The incidence of ILD appeared to be higher in Asian patients (2.3%; 38/1657) as compared to Whites (1.0%; 23/2241). In LUX-Lung 3, the incidence of Grade ≥3 ILD was 1.3% and resulted in death in 1% of GILOTRIF-treated patients. In LUX-Lung 8, the incidence of Grade ≥3 ILD was 0.9% and resulted in death in 0.8% of GILOTRIF-treated patients. Withhold GILOTRIF during evaluation of patients with suspected ILD, and discontinue GILOTRIF in patients with confirmed ILD. **Hepatic Toxicity:** In 4257 patients who received GILOTRIF across clinical trials, 9.7% had liver test abnormalities, of which 0.2% were fatal. In LUX-Lung 3, liver test abnormalities of any grade occurred in 17.5% of the patients treated with GILOTRIF, of which 3.5% had Grade 3-4 liver test abnormalities. In LUX-Lung 8, liver test abnormalities of any grade occurred in 6% of the patients treated with GILOTRIF, of which 0.2% had Grade 3-4 liver test abnormalities. Obtain periodic liver testing in patients during treatment with GILOTRIF. Withhold GILOTRIF in patients who develop worsening of liver function. In patients who develop severe hepatic impairment while taking GILOTRIF, treatment should be discontinued. **Gastrointestinal Perforation:** Gastrointestinal perforation, including fatal cases, has occurred with GILOTRIF. Gastrointestinal perforation has been reported in 0.2% of patients treated with GILOTRIF among 3213 patients across 17 randomized controlled clinical trials. Patients receiving concomitant corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs) or anti-angiogenic agents, or patients with increasing age or who have an underlying history of gastrointestinal ulceration, underlying diverticular disease or bowel metastases may be at increased risk of perforation. Permanently discontinue GILOTRIF in patients who develop gastrointestinal perforation. **Keratitis:** Keratitis, characterized as acute or worsening eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain, and/or red eye occurred in 0.7% of patients treated with GILOTRIF among 4257 patients across clinical trials, of which 0.05% of patients experienced Grade 3 keratitis. Keratitis was reported in 2.2% patients in LUX-Lung 3, with Grade 3 in 0.4%. In LUX-Lung 8, keratitis was reported in 0.3% patients; there were no patients with ≥Grade 3 keratitis. Withhold GILOTRIF during evaluation of patients with suspected keratitis, and if diagnosis of ulcerative keratitis is confirmed, treatment with GILOTRIF should be interrupted or discontinued. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered. GILOTRIF should be used with caution in patients with a history of keratitis, ulcerative keratitis, or severe dry eye *[see Adverse Reactions]*. Contact lens use is also a risk factor for keratitis and ulceration. **Embryo-Fetal Toxicity:** Based on findings from animal studies and its mechanism of action, GILOTRIF can cause fetal harm when administered to a pregnant woman. Administration of afatinib to pregnant rabbits during organogenesis at exposures approximately 0.2 times the exposure in humans at the recommended dose of 40 mg daily resulted in embryotoxicity and, in rabbits showing maternal toxicity, increased abortions at late gestational stages. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment, and for at least 2 weeks after the last dose of GILOTRIF.

ADVERSE REACTIONS: The following adverse reactions are discussed in greater detail in other sections of the labeling: Diarrhea *[see Warnings and Precautions]*; Bullous and Exfoliative Skin Disorders *[see Warnings and Precautions]*; Interstitial Lung Disease *[see Warnings and Precautions]*; Hepatic Toxicity *[see Warnings and Precautions]*; Keratitis *[see Warnings and Precautions]*. **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 reflect exposure to GILOTRIF for clinically significant adverse reactions in 4257 patients enrolled in LUX-Lung 3 (n=229) and LUX-Lung 8 (n=392), and 3636 patients with cancer enrolled in 42 studies of GILOTRIF administered alone or in combination with other anti-neoplastic drugs at GILOTRIF doses ranging from 10-70 mg daily or at doses 10-160 mg in other regimens. The mean exposure was 5.5 months. The population included patients with various cancers, the most common of which were NSCLC, breast, colorectal, brain, and head and neck. The data described below reflect exposure to GILOTRIF as a single agent in LUX-Lung 3, a randomized, active-controlled trial conducted in patients with EGFR mutation-positive, metastatic NSCLC, and in LUX-Lung 8, a randomized, active-controlled trial in patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy. EGFR Mutation-Positive, Metastatic NSCLC: The data in Tables 1 and 2 below reflect the exposure of 229 EGFR-tyrosine kinase inhibitor-naïve, GILOTRIF-treated patients with EGFR mutation-positive, metastatic, non-squamous NSCLC enrolled in a randomized, multicenter, open-label trial (LUX-Lung 3). Patients received GILOTRIF 40 mg daily until documented disease progression or intolerance to the therapy. A total of 111 patients were treated with pemetrexed/cisplatin. Patients were treated with pemetrexed 500 mg/m^2 followed after 30 minutes by cisplatin 75 mg/m^2 every three weeks for a maximum of six treatment courses. The median exposure was 11 months for patients treated with GILOTRIF and 3.4 months for patients treated with pemetrexed/cisplatin. The overall trial population had a median age of 61 years; 61% of patients in the GILOTRIF arm and 60% of patients in the pemetrexed/cisplatin arm were younger than 65 years. A total of 64% of patients on GILOTRIF and 67% of pemetrexed/cisplatin patients were female. More than two-thirds of patients were from Asia (GILOTRIF 70%; pemetrexed/cisplatin 72%). Serious adverse reactions were reported in 29% of patients treated with GILOTRIF. The most frequent serious adverse reactions reported in patients treated with GILOTRIF were diarrhea (6.6%); vomiting (4.8%); and dyspnea, fatigue, and hypokalemia (1.7% each). Fatal adverse reactions in GILOTRIF-treated patients in LUX-Lung 3 included pulmonary toxicity/ILD-like adverse reactions (1.3%), sepsis (0.43%), and pneumonia (0.43%). Dose reductions due to adverse reactions were required in 57% of GILOTRIF-treated patients. The most frequent adverse reactions that led to dose reduction in the patients treated with GILOTRIF were diarrhea (20%), rash/acne (19%), paronychia (14%), and stomatitis (10%). Discontinuation of therapy in GILOTRIF-treated patients for adverse reactions was 14.0%. The most frequent adverse reactions that led to discontinuation in GILOTRIF-treated patients were diarrhea (1.3%), ILD (0.9%), and paronychia (0.9%). Clinical trials of GILOTRIF excluded patients with an abnormal left ventricular ejection fraction (LVEF), i.e., below the institutional lower limit of normal. In LUX-Lung 3, all patients were evaluated for LVEF at screening and every 9 weeks thereafter in the GILOTRIF-treated group and as needed in the pemetrexed/cisplatin group. More GILOTRIF-treated patients (2.2%; n=5) experienced ventricular dysfunction (defined as diastolic dysfunction, left ventricular dysfunction, or ventricular dilation; all < Grade 3) compared to chemotherapy-treated patients (0.9%; n=1). Tables 1 and 2 summarize common adverse reactions and laboratory abnormalities in LUX-Lung 3.

Table 1 Adverse Reactions Reported in ≥10% of GILOTRIF-Treated Patients in LUX-Lung 3*

Adverse Reaction	GILOTRIF n=229		Pemetrexed/ Cisplatin n=111	
	All Grades (%)	Grade 3† (%)	All Grades (%)	Grade 3† (%)
Gastrointestinal disorders				
Diarrhea	96	15	23	2
Stomatitis[1]	71	9	15	1
Cheilitis	12	0	1	0
Skin and subcutaneous tissue disorders				
Rash/ acneiform dermatitis[2]	90	16	11	0
Pruritus	21	0	1	0
Dry skin	31	0	2	0
Infections				
Paronychia[3]	58	11	0	0
Cystitis	13	1	5	0
Respiratory, thoracic and mediastinal disorders				
Epistaxis	17	0	2	1
Rhinorrhea	11	0	6	0
Investigations				
Weight decreased	17	1	14	1
General disorders and administration site conditions				
Pyrexia	12	0	6	0
Eye disorders				
Conjunctivitis	11	0	3	0

*NCI CTCAE v 3.0

†None of the adverse reactions in this table except stomatitis (one patient on GILOTRIF [0.4%]) were Grade 4 in severity.

[1]Includes stomatitis, aphthous stomatitis, mucosal inflammation, mouth ulceration, oral mucosa erosion, mucosal erosion, mucosal ulceration

[2]Includes acne, acne pustular, dermatitis, acneiform dermatitis, dermatosis, drug eruption, erythema, exfoliative rash, folliculitis, rash, rash erythematous, rash follicular, rash generalized, rash macular, rash maculo-papular, rash pruritic, rash pustular, skin disorder, skin erosion, skin exfoliation, skin fissures, skin lesion, skin reaction, skin toxicity, skin ulcer

[3]Includes paronychia, nail infection, nail bed infection

Other clinically important adverse reactions observed in patients treated with GILOTRIF but that occurred at a higher incidence in pemetrexed/cisplatin-treated patients and not listed elsewhere in section 6 include: decreased appetite (29% Grades 1-4, 4% Grade 3), nausea (25% Grades 1-4, 4% Grade 3), and vomiting (23% Grades 1-4, 4% Grade 3).

Table 2 Laboratory Abnormalities Occurring in ≥10% of GILOTRIF Arm and at ≥2% Higher Incidence than in Chemotherapy Arm in LUX-Lung 3*

Laboratory Abnormality	GILOTRIF n=229		Pemetrexed/ Cisplatin n=111	
	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
Increased alanine aminotransferase (ALT)	54	2	27	1
Increased alkaline phosphate	51	3	46	1
Decreased creatinine clearance	49	2	47	1
Increased aspartate aminotransferase (AST)	46	3	22	1
Decreased lymphocytes	38	9	32	14
Decreased potassium	30	8	11	3
Increased bilirubin	16	1	8	0

*NCI CTCAE v 3.0

Previously Treated, Metastatic Squamous NSCLC: The safety of GILOTRIF was evaluated in 392 GILOTRIF-treated patients with metastatic squamous NSCLC enrolled in a randomized, multicenter, open-label trial (LUX-Lung 8). Patients were required to have received at least four cycles of platinum-based chemotherapy, ECOG Performance Status (PS) 0 or 1, and normal left ventricular ejection fraction (LVEF). Patients received GILOTRIF 40 mg once daily (n=392) or erlotinib 150 mg once daily (n=395). Treatment continued until documented disease progression or intolerance to the therapy. Among the 392 GILOTRIF-treated patients, the median age was 65 years, 53% were 65 years of age or older, 84% were male, 72% were White, 25% were Asian, ECOG PS 0 (32%) or 1 (68%). The median exposure was 2.1 months for patients treated with GILOTRIF, 15% were exposed for at least 6 months, and 5% were exposed for at least 12 months. Serious adverse reactions occurred in 44% of patients treated with GILOTRIF. The most frequent serious adverse reactions in patients treated with GILOTRIF were pneumonia (6.6%), diarrhea (4.6%), and dehydration and dyspnea (3.1% each). Fatal adverse reactions in GILOTRIF-treated patients included ILD (0.5%), pneumonia (0.3%), respiratory failure (0.3%), acute renal failure (0.3%), and general physical health deterioration (0.3%). Dose reductions due to adverse reactions were required in 27% of GILOTRIF-treated patients and discontinuation of GILOTRIF for adverse reactions was required for 20%. The most frequent adverse reactions that led to dose reduction in the patients treated with GILOTRIF were diarrhea (15%), rash/acne (5.9%), and stomatitis (3.1%). The most frequent adverse reactions that led to discontinuation in GILOTRIF-treated patients were diarrhea (4.1%) and rash/acne (2.6%). Tables 3 and 4 summarize common adverse reactions and laboratory abnormalities in LUX-Lung 8.

Table 3 Adverse Reactions Reported in ≥10% of GILOTRIF-Treated Patients in LUX-Lung 8*

Adverse Reaction	GILOTRIF n=392		Erlotinib n=395	
	All Grades (%)	Grade 3-4 (%)	All Grades (%)	Grade 3-4 (%)
Gastrointestinal disorders				
Diarrhea	75	11	41	3
Stomatitis[1]	30	4	11	1
Nausea	21	2	16	1
Vomiting	13	1	10	1
Skin and subcutaneous tissue disorders				
Rash/acneiform dermatitis[2]	70	7	70	11
Pruritus	10	0	13	0
Infections				
Paronychia[3]	11	1	5	0
Metabolism and nutrition disorders				
Decreased appetite	25	3	26	2

*NCI CTCAE v 3.0

[1]Includes stomatitis, aphthous stomatitis, mucosal inflammation, mouth ulceration, oral mucosa erosion, mucosal erosion, mucosal ulceration

[2]Includes acne, dermatitis, acneiform dermatitis, eczema, erythema, exfoliative rash, folliculitis, rash, rash generalized, rash macular, rash maculo-papular, rash pruritic, rash pustular, skin exfoliation, skin fissures, skin lesion, skin reaction, skin toxicity, skin ulcer

[3]Includes paronychia, nail infection, nail bed infection

Table 4 Laboratory Abnormalities Occurring in ≥10% of GILOTRIF Arm and at ≥2% Higher Incidence than in Erlotinib Arm in LUX-Lung 8*

Laboratory Abnormality	GILOTRIF n=392		Erlotinib n=395	
	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
Increased alkaline phosphate	34	2	31	0
Decreased white blood cell count	12	1	8	1
Decreased potassium	11	1	8	1

*NCI CTCAE v 3.0

Other clinically important laboratory abnormalities observed in patients treated with GILOTRIF that are not listed in Table 4 are: increased alanine aminotransferase (10% Grade 1-4; 1% Grade 3-4), increased aspartate aminotransferase (7% Grade 1-4; 1% Grade 3-4), and increased bilirubin (3% Grade 1-4; 0 Grade 3-4). *Less Common Adverse Reactions:* Other adverse reactions reported in patients treated with GILOTRIF in LUX-Lung 3 and LUX-Lung 8 include: *Skin and subcutaneous disorders:* nail disorders occurred in 9.2% and 2.8% of patients, respectively. **Postmarketing Experience:** The following adverse reactions have been identified during post-approval use of GILOTRIF. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: Pancreatitis; Toxic epidermal necrolysis/Stevens Johnson syndrome.

DRUG INTERACTIONS: *Effect of P-glycoprotein (P-gp) Inhibitors and Inducers:* Concomitant taking of P-gp inhibitors (including but not limited to ritonavir, cyclosporine A, ketoconazole, itraconazole, erythromycin, verapamil, quinidine, tacrolimus, nelfinavir, saquinavir, and amiodarone) with GILOTRIF can increase exposure to afatinib. Concomitant taking of P-gp inducers (including but not limited to rifampicin, carbamazepine, phenytoin, phenobarbital, and St. John's wort) with GILOTRIF can decrease exposure to afatinib.

USE IN SPECIFIC POPULATIONS: Pregnancy: *Risk Summary:* Based on findings from animal studies and its mechanism of action, GILOTRIF can cause fetal harm when administered to a pregnant woman. There are no available data on the use of GILOTRIF in pregnant women. Administration of afatinib to pregnant rabbits during organogenesis at exposures approximately 0.2 times the exposure in humans at the recommended dose of 40 mg daily resulted in embryotoxicity and, in rabbits showing maternal toxicity, increased abortions at late gestational stages *[see Data]*. Advise a pregnant woman of the potential risk to a fetus. The background risk of major birth defects and miscarriage for the indicated population is unknown. 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 rabbits, administration of afatinib to pregnant animals at doses of 5 mg/kg (approximately 0.2 times the exposure by AUC at the recommended human dose of 40 mg daily) or greater during the period of organogenesis caused increased post-implantation loss, and in animals showing maternal toxicity, abortion at late gestational stages. In the same study, at the high dose level of 10 mg/kg (approximately 0.7 times the exposure by AUC at the recommended human dose of 40 mg daily), there were reduced fetal weights, and increases in the incidence of runts, as well as visceral and dermal variations. In an embryo-fetal development study in rats, there were skeletal alterations consisting of incomplete or delayed ossifications and reduced fetal weight at a dose of 16 mg/kg (approximately twice the exposure based on AUC at the recommended human dose of 40 mg daily). **Lactation:** *Risk Summary:* There are no data on the presence of afatinib in human milk or its effects on the breastfed infant or on milk production. Afatinib was present in the milk of lactating rats *[see Data]*. Because of the potential for serious adverse reactions in nursing infants from GILOTRIF, advise a lactating woman not to breastfeed during treatment with GILOTRIF and for 2 weeks after the final dose. *Data:* Afatinib was present in the milk of lactating rats at concentrations 80 and 150 times higher than those found in plasma at 1 and 6 hours after administration. **Females and Males of Reproductive Potential:** *Contraception:* Females: GILOTRIF can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with GILOTRIF, and for at least 2 weeks after the last dose of GILOTRIF *[see Use in Specific Populations]. Infertility:* Based on results from an animal fertility study, GILOTRIF may reduce fertility in females and males of reproductive potential. It is not known if the effects on fertility are reversible. **Pediatric Use:** Safety and effectiveness of GILOTRIF in pediatric patients have not been established. **Geriatric Use:** LUX-Lung 3 did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In LUX-Lung 8, 53% of the 398 patients randomized to receive afatinib were 65 years of age or older and 11% were 75 years or older. In an exploratory subgroup analysis of LUX-Lung 8, the hazard ratio for overall survival (OS) in patients less than 65 years old was 0.68 (95% CI: 0.55, 0.85) and in patients 65 years or older was 0.95 (95% CI: 0.76, 1.19). No overall differences in safety were observed between patients 65 years and older and younger patients. **Renal Impairment:** Patients with severe renal impairment have a higher exposure to afatinib than patients with normal renal function. Administer GILOTRIF at a starting dose of 30 mg once daily in patients with severe renal impairment. Adjustments to the starting dose of GILOTRIF are not necessary in patients with mild or moderate renal impairment. Dosing recommendations for patients with eGFR <15 mL/min/1.73 m^2 or on dialysis cannot be provided as GILOTRIF has not been studied in these patient populations. **Hepatic Impairment:** GILOTRIF has not been studied in patients with severe (Child Pugh C) hepatic impairment. Adjustments to the starting dose of GILOTRIF are not necessary in patients with mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment. Closely monitor patients with severe hepatic impairment and adjust GILOTRIF dose if not tolerated.

OVERDOSAGE Overdose was reported in 2 healthy adolescents each of whom ingested 360 mg of GILOTRIF (as part of a mixed-drug ingestion) resulting in nausea, vomiting, asthenia, dizziness, headache, abdominal pain, and elevated amylase [<1.5 times upper limit of normal (ULN)]. Both subjects recovered.

PATIENT COUNSELING INFORMATION: *See FDA-approved patient labeling (Patient Information).* Diarrhea: Advise patients that diarrhea occurs in nearly all patients who receive GILOTRIF. Inform patients that diarrhea may result in dehydration and renal impairment if not treated. Advise patients to notify their physician if diarrhea develops and to seek medical attention promptly for severe or persistent diarrhea *[see Warnings and Precautions and Adverse Reactions]*. Bullous and Exfoliative Skin Disorders: Advise patients to minimize sun exposure with protective clothing and use of sunscreen while taking GILOTRIF *[see Warnings and Precautions]*. Interstitial Lung Disease: Advise patients to immediately report any new or worsening lung symptoms, or any combination of the following symptoms: trouble breathing or shortness of breath, cough, fever *[see Warnings and Precautions]*. Hepatic Toxicity: Advise patients that they will need to undergo liver function monitoring periodically. Advise patients to immediately report any symptoms of a liver problem [e.g., skin or the whites of eyes turn yellow, urine turns dark or brown (tea colored), pain on the right side of stomach, bleeds or bruises more easily than normal, lethargy] *[see Warnings and Precautions]*. Keratitis: Advise patients to immediately report eye problems (e.g., eye pain, swelling, redness, blurred vision, or other vision changes) *[see Warnings and Precautions]*. Left Ventricular Dysfunction: Advise patients to contact a healthcare professional immediately for any of the following: new onset or worsening shortness of breath or exercise intolerance, cough, fatigue, swelling of the ankles/legs, palpitations, or sudden weight gain *[see Adverse Reactions]*. Instructions for Taking GILOTRIF: Advise patients to take GILOTRIF on an empty stomach at least 1 hour before or 2 hours after eating. Advise patients not to take a missed dose within 12 hours of the next dose. Embryo-Fetal Toxicity: Advise pregnant women and females of reproductive potential that GILOTRIF can result in fetal harm. Advise female patients to contact their healthcare provider with a known or suspected pregnancy. Advise females of reproductive potential to use effective contraception during treatment with GILOTRIF and for at least 2 weeks after the last dose of GILOTRIF *[see Use in Specific Populations]*. Lactation: Advise women not to breastfeed during treatment with GILOTRIF and for 2 weeks after the last dose of GILOTRIF *[see Use in Specific Populations]*; Infertility: Advise females and males of reproductive potential of the potential for reduced fertility from GILOTRIF *[see Use in Specific Populations]*.

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Boehringer Ingelheim

LEADERSHIP APPOINTMENTS

John Mills
Vice President of Pharmacy Services

With daily oversight of all pharmacy services for the FCS Oral Oncolytic Specialty Pharmacy, Rx To Go, John actively supports pharmacy operations and future expansion activities. He joined FCS in 2019 as Director of Payer Relations and Business Strategy and was promoted to Senior Director of Pharmacy the following year. He has been influential in strengthening our payer relationships, which has enabled our in-house pharmacy to serve more patients, eliminating delays in treatment.

NEW PHYSICIANS JOIN FCS

Cesar Perez, MD
Medical Oncologist
Lake Nona

Gilberto de Almeida Rodrigues, MD, MS
Medical Oncologist/ Hematologist
Lake City

Rx TO GO
Your In-House Pharmacy at Florida Cancer Specialists

Oral Oncolytic Pharmacy Earns Dual NABP Pharmacy Accreditations

Our FCS in-house oral oncolytic pharmacy, Rx To Go, has been accredited by the National Association of Boards of Pharmacy® (NABP®) for both specialty pharmacy and digital pharmacy practice.

These accreditations recognize FCS for providing an advanced level of pharmacy services and disease management for patients taking medications that require special handling, storage and distribution, and for our commitment to quality healthcare and safe pharmacy practices over the internet.

We congratulate our entire Pharmacy team on achieving this impressive recognition for demonstrated compliance to a comprehensive set of best practice standards.

NABP Accredited Specialty Pharmacy

NABP Accredited Digital Pharmacy

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Please see full prescribing information for Fulvestrant at fresenius-kabi.com/us.

FCS Foundation News & Events

For tickets and sponsorship information, visit FCSF.org/Events

10 YEARS of hope | FLORIDA CANCER SPECIALISTS Foundation

Service & Support. Healing & Hope.

"The effort and kindness shown to me during a highly stressful time while having treatments were genuinely unique. To have this dedicated, professional and compassionate group working 100% on my behalf is something I will never forget. They changed my life. There is such a significant need for assistance, and my prayer is to one day be able to donate/give back/volunteer with FCS Foundation, so they can continue their mission for others as they did for me. I love them all!"

— *Sandra McClendon*

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Benefiting Florida Cancer Specialists Foundation

Wine Women & Shoes
March 26, 2022, Ritz-Carlton Resort, Naples

FCS FOUNDATION 3RD ANNUAL FARM TO TABLE

Farm to Table
January 29, 2022, Patel Oaks Farm, Ocala

Party UNDER THE Stars

A Different Kind of Maskerade
Party Under the Stars
February 26, 2022, Hyatt Regency, Sarasota

Lyrics for Life
March 4, 2022, Phillips Center, Gainesville

FLORIDA CANCER SPECIALISTS Foundation

The Florida Cancer Specialists Foundation is a 501(c)3 nonprofit organization that helps individuals with their essential living expenses while they undergo treatment for cancer. Cancer patients are able to receive assistance from the Foundation for their non-medical bills, such as overdue rent, mortgage, utility bills and car payments. This financial assistance immediately impacts cancer patients and their families in communities throughout Florida, allowing them to focus on their recovery.

From Our Patients

★★★★★

GOOGLE REVIEW: 5 STARS

Rina Patel, MD

It is with utter gratitude that my family and I write this note to express our immense respect and appreciation for Dr. Rina Patel, who helped our mom overcome cancer. For the past 12-plus months, Dr. Patel has been treating Mom with the highest level of medical support, extraordinary bed-manners, kindness, patience and timely communication at times when things got rough and very scary for us. We wanted the rest of the world to know about Dr. Rina Patel for such excellence in combining ethics, patient care and respect, wisdom and advanced knowledge is a rare phenomenon in our days. Thank you, Dr. Patel, for saving Mom's life.

★★★★★

GOOGLE REVIEW: 5 STARS

Nuruddin Jooma, MD, MPH

From my first visit with Dr. Jooma at the Highland office, everyone has been so caring, patient and compassionate. When I needed a PET scan and my veins were not cooperating, they brought me a blanket and a bottled water. They gave me time to compose myself when the tears came. Most importantly, they gently encouraged me to let them try one last time to find a cooperative vein when I was at my wits end and ready to give up. It worked, and I was able to get my scan done.

★★★★★

GOOGLE REVIEW: 5 STARS

Guillermo Abesada-Terk Jr., MD

Nobody wants to go through the experience of cancer treatment. Very much to my delight, I came across Florida Cancer Specialists. Dr. Abesada and his staff are absolutely extraordinary. From the moment you walk through the door, the receptionists are kind, efficient and caring with a smile. You would think every staff member, nurse, etc., are handpicked professionals who make you feel as comfortable as anybody could feel. … I don't think I could receive better care any place on the Treasure Coast. I have all of the confidence in the world these people will heal me.

★★★★★

GOOGLE REVIEW: 5 STARS

Elizabeth Byron, MD

I met Dr. Byron in November 2020. She was very knowledgeable about my situation. That's what I liked about her. She was always trying new clinical trials and continued to learn more. She answered my questions, and I didn't feel rushed. She told me, "We will get through this," and we did. On May 17, she went over my results, and I am cancer free! I still have a journey to go, but with God and her staff, I know we will get there.

★★★★★

GOOGLE REVIEW: 5 STARS

Antonella Leary, MD

Dr. Leary is one amazing doctor in her field. She is warm, friendly and very compassionate. I will also say that her nurse practitioner, Sarah Fleming, is such a kind person. I wish I could give more than five stars because they deserve a lot more then five. Thank you for all the wonderful care you give.

★★★★★

GOOGLE REVIEW: 5 STARS

Elisabeth McKeen, MD

Five stars are not enough! Her knowledge, patience and caring qualities are what made me feel confident and safe at one of the darkest times in my life. I am thankful every day that someone recommended her to me.

★★★★★

GOOGLE REVIEW: 5 STARS

Hitesh Patel, MD

Best man for the job. Got my mom an extra two years. Thank you for what you do for people in need. If I had the same issues, I know who I am calling.

Have something to add?

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

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