FCS THE MAGAZINE

FALL/WINTER 2022

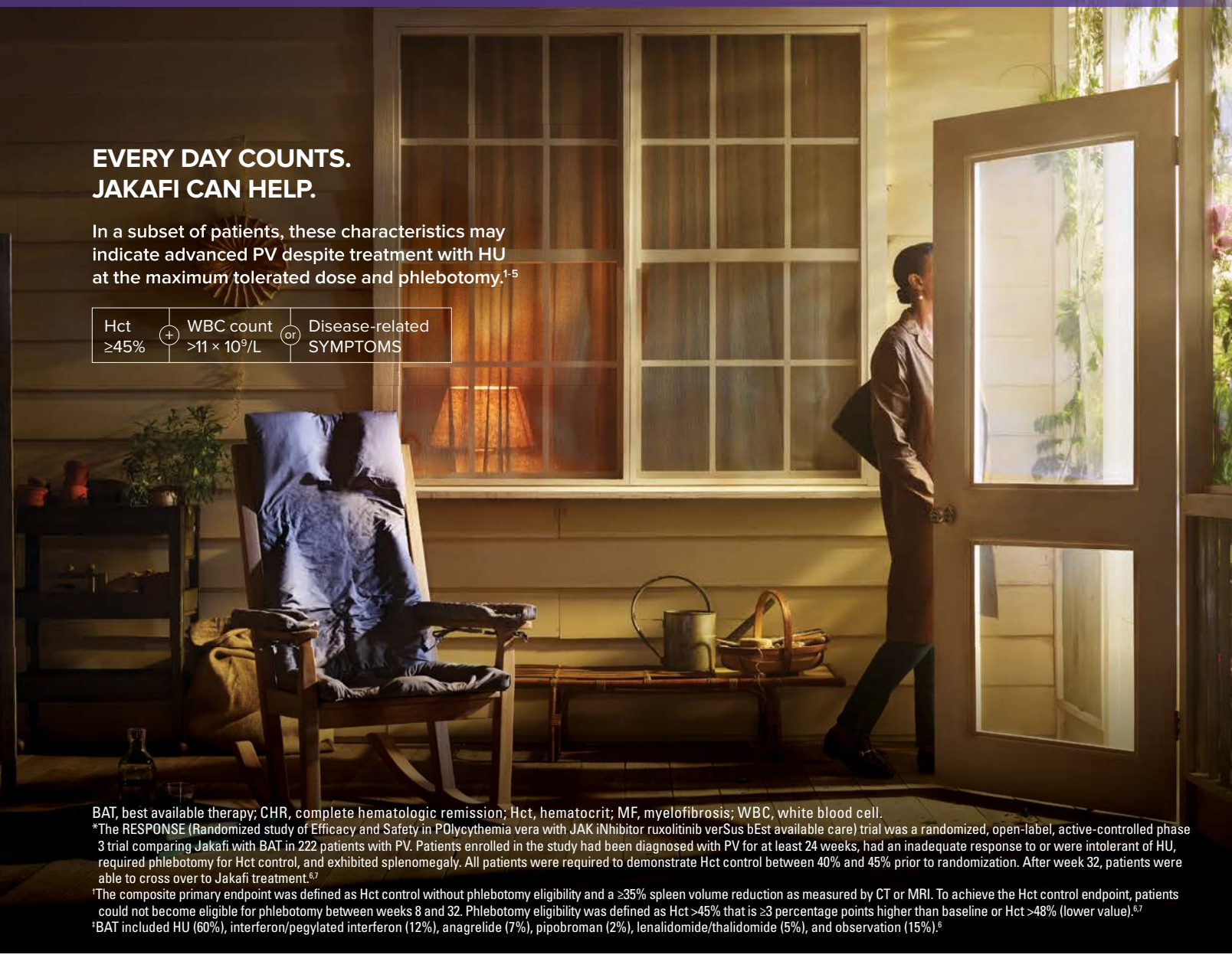
# A Family Affair

## Three siblings carve individual career paths at FCS

FLORIDA CANCER SPECIALISTS & Research Institute

ION Oncology Practice Network

**For adults with polycythemia vera (PV) who have had an inadequate response to or are intolerant of hydroxyurea (HU)**



## EVERY DAY COUNTS. JAKAFI CAN HELP.

In a subset of patients, these characteristics may indicate advanced PV despite treatment with HU at the maximum tolerated dose and phlebotomy.[1-5]

| Hct ≥45% | + | WBC count >11 × $10^9$/L | or | Disease-related SYMPTOMS |
|---|---|---|---|---|

BAT, best available therapy; CHR, complete hematologic remission; Hct, hematocrit; MF, myelofibrosis; WBC, white blood cell.

*The RESPONSE (Randomized study of Efficacy and Safety in POlycythemia vera with JAK iNhibitor ruxolitinib verSus bEst available care) trial was a randomized, open-label, active-controlled phase 3 trial comparing Jakafi with BAT in 222 patients with PV. Patients enrolled in the study had been diagnosed with PV for at least 24 weeks, had an inadequate response to or were intolerant of HU, required phlebotomy for Hct control, and exhibited splenomegaly. All patients were required to demonstrate Hct control between 40% and 45% prior to randomization. After week 32, patients were able to cross over to Jakafi treatment.[6,7]

†The composite primary endpoint was defined as Hct control without phlebotomy eligibility and a ≥35% spleen volume reduction as measured by CT or MRI. To achieve the Hct control endpoint, patients could not become eligible for phlebotomy between weeks 8 and 32. Phlebotomy eligibility was defined as Hct >45% that is ≥3 percentage points higher than baseline or Hct >48% (lower value).[6,7]

‡BAT included HU (60%), interferon/pegylated interferon (12%), anagrelide (7%), pipobroman (2%), lenalidomide/thalidomide (5%), and observation (15%).[6]

### Indications and Usage

Jakafi is indicated for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea.

### Important Safety Information

- Treatment with Jakafi® (ruxolitinib) can cause thrombocytopenia, anemia and neutropenia, which are each dose-related effects. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated
- Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary
- Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi
- Severe neutropenia (ANC <0.5 × $10^9$/L) was generally reversible by withholding Jakafi until recovery
- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines
- Tuberculosis (TB) infection has been reported. Observe patients taking Jakafi for signs and symptoms of active TB and manage promptly. Prior to initiating Jakafi, evaluate patients for TB risk factors and test those at higher risk for latent infection. Consult a physician with expertise in the treatment of TB before starting Jakafi in patients with evidence of active or latent TB. Continuation of Jakafi during treatment of active TB should be based on the overall risk-benefit determination
- Progressive multifocal leukoencephalopathy (PML) has occurred with Jakafi treatment. If PML is suspected, stop Jakafi and evaluate
- Advise patients about early signs and symptoms of herpes zoster and to seek early treatment
- Increases in hepatitis B viral load with or without associated elevations in alanine aminotransferase and aspartate aminotransferase have been reported in patients with chronic hepatitis B virus (HBV) infections. Monitor and treat patients with chronic HBV infection according to clinical guidelines
- When discontinuing Jakafi, myeloproliferative neoplasm-related symptoms may return within one week. After discontinuation, some patients with myelofibrosis have experienced fever, respiratory distress, hypotension, DIC, or multi-organ failure. If any of these occur after discontinuation or while tapering Jakafi, evaluate and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi without consulting their physician. When discontinuing or interrupting Jakafi for reasons other than thrombocytopenia or neutropenia, consider gradual tapering rather than abrupt discontinuation
- Non-melanoma skin cancers (NMSC) including basal cell, squamous cell, and Merkel cell carcinoma have occurred. Perform periodic skin examinations
- Treatment with Jakafi has been associated with increases in total cholesterol, low-density lipoprotein cholesterol, and triglycerides. Assess lipid parameters 8-12 weeks after initiating Jakafi. Monitor and treat according to clinical guidelines for the management of hyperlipidemia
- Another JAK-inhibitor has increased the risk of major adverse cardiovascular events (MACE), including cardiovascular death, myocardial infarction, and stroke (compared to those treated with tumor TNF

## INTERVENE WITH JAKAFI TO ACHIEVE DURABLE COUNT CONTROL

In the phase 3 RESPONSE* trial, Jakafi demonstrated superior results† vs BAT‡

### Composite Primary Endpoint

**23%** (25/110) of patients receiving Jakafi achieved Hct control and ≥35% spleen volume reduction at week 32 vs <1% (1/112) of patients receiving BAT ($P < 0.0001$)[6§]

§Jakafi 95% CI, 0.15-0.32; BAT 95% CI, 0.00-0.05.[6]

### Individual Component of the Primary Endpoint

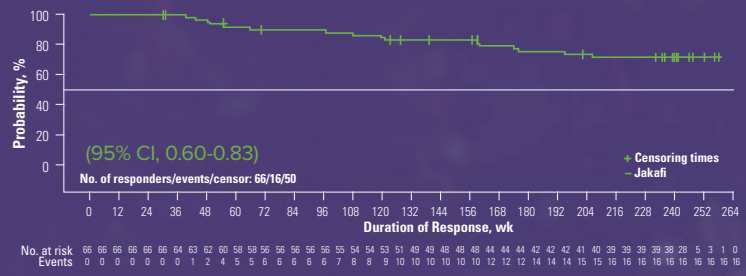
**60%** (66/110) of patients receiving Jakafi achieved Hct control at week 32 vs 19% (21/112) of patients receiving BAT[6]

To achieve the Hct control endpoint, patients could not become eligible for phlebotomy between weeks 8 and 32. Phlebotomy eligibility was defined as Hct >45% that is ≥3 percentage points higher than baseline or Hct >48% (lower value)[6,7]

**73%** **Probability of Maintaining Hct Control[a] at 5 Years in RESPONSE Trial[8,9]**

[a]Absence of phlebotomy eligibility

**Kaplan-Meier Estimate: Durability of Hct Control at 5 Years**




- Analysis was conducted in week 32 Hct control responders, beginning at week 32[8]
- Progression events for the evaluation of duration of absence of phlebotomy eligibility included first of 2 consecutive Hct assessments that confirms phlebotomy eligibility, death, or development of MF or acute leukemia[10]

Reprinted from *The Lancet Haematology*, 7(3), Kiladjian J-J, Zachee P, Hino M, et al, Long-term efficacy and safety of ruxolitinib versus best available therapy in polycythaemia vera (RESPONSE): 5-year follow up of a phase 3 study, e226-e237, Copyright 2020, with permission from Elsevier.

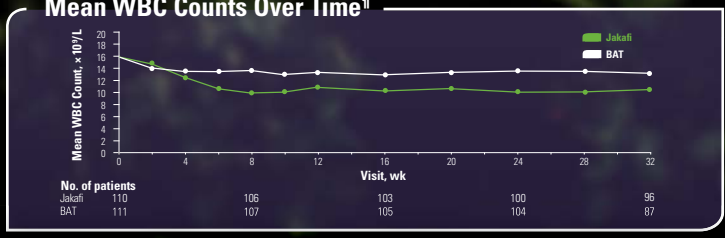
### Secondary Endpoint

**24%** (26/110) of patients receiving Jakafi achieved the secondary endpoint of CHR at week 32 vs 8% (9/112) of patients receiving BAT ($P = 0.0016$)[6‖]

‖Jakafi 95% CI, 0.16-0.33; BAT 95% CI, 0.04-0.15.

### Exploratory Analysis From the RESPONSE Trial[11]

**Mean WBC Counts Over Time¶**




¶Jakafi reduced mean WBCs as an individual component of CHR. CHR was defined as achieving Hct control (as specified in the primary endpoint), platelet count ≤400 × $10^9$/L, and WBC count ≤$10^9$/L.[6,7]

**Intervene with Jakafi in your appropriate patients with advanced PV**
**SWITCHTOJAKAFI.COM**

Jakafi® ruxolitinib (tablets)
5mg • 10mg • 15mg • 20mg • 25mg

blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur

- Another JAK-inhibitor has increased the risk of thrombosis, including deep venous thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. In patients with myelofibrosis (MF) and polycythemia vera (PV) treated with Jakafi in clinical trials, the rates of thromboembolic events were similar in Jakafi and control treated patients. Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately
- Another JAK-inhibitor has increased the risk of lymphoma and other malignancies excluding NMSC (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi, particularly in patients with a known secondary malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers
- In myelofibrosis and polycythemia vera, the most common nonhematologic adverse reactions (incidence ≥15%) were bruising, dizziness, headache, and diarrhea. In acute graft-versus-host disease, the most common nonhematologic adverse reactions (incidence >50%) were infections (pathogen not specified) and edema. In chronic graft-versus-host disease, the most common nonhematologic adverse reactions (incidence ≥20%) were infections (pathogen not specified) and viral infections
- Avoid concomitant use with fluconazole doses greater than 200 mg. Dose modifications may be required when administering Jakafi with fluconazole doses of 200 mg or less, or with strong CYP3A4 inhibitors, or in patients with renal or hepatic impairment. Patients should be closely monitored and the dose titrated based on safety and efficacy
- Use of Jakafi during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus. Women taking Jakafi should not breastfeed during treatment and for 2 weeks after the final dose

Please see Brief Summary of Full Prescribing Information for Jakafi on the following pages. To learn more about Jakafi, visit **HCP.Jakafi.com**

**References: 1.** Barosi G, et al. *Br J Haematol.* 2010;148(6):961-963. **2.** Marchioli R, et al. *N Engl J Med.* 2013;368(1):22-33. **3.** Barbui T, et al. *Blood.* 2015;126(4):560-561. **4.** Emanuel RM, et al. *J Clin Oncol.* 2012;30(33):4098-4103. **5.** Verstovsek S, et al. *Cancer.* 2014;120(4):513-520. **6.** Jakafi Prescribing Information. Wilmington, DE: Incyte Corporation. **7.** Vannucchi AM, et al. *N Engl J Med.* 2015;372(5):426-435. **8.** Kiladjian J-J, et al. *Lancet Haematol.* 2020;7(3):e226-e237. **9.** Kiladjian J-J, et al. *Lancet Haematol.* 2020;7(Suppl):1-18. **10.** Data on file. Incyte Corporation. Wilmington, DE. **11.** Vannucchi AM, et al. *N Engl J Med.* 2015;372(Suppl):1-25.



Incyte

Jakafi®
ruxolitinib (tablets)
5mg • 10mg • 15mg • 20mg • 25mg

**BRIEF SUMMARY:** For Full Prescribing Information, see package insert.

**INDICATIONS AND USAGE Myelofibrosis** Jakafi is indicated for treatment of intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF in adults. **Polycythemia Vera** Jakafi is indicated for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea. **Acute Graft-Versus-Host Disease** Jakafi is indicated for treatment of steroid-refractory acute graft-versus-host disease (aGVHD) in adult and pediatric patients 12 years and older. **Chronic Graft-Versus-Host Disease** Jakafi is indicated for treatment of chronic graft-versus-host disease (cGVHD) after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older.

**CONTRAINDICATIONS** None.

**WARNINGS AND PRECAUTIONS Thrombocytopenia, Anemia and Neutropenia** Treatment with Jakafi can cause thrombocytopenia, anemia and neutropenia. *[see Adverse Reactions (6.1) in Full Prescribing Information]*. Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary *[see Dosage and Administration (2) in Full Prescribing Information]*. Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi. Severe neutropenia (ANC less than $0.5 \times 10^9$/L) was generally reversible by withholding Jakafi until recovery. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated *[see Dosage and Administration (2) in Full Prescribing Information]*. **Risk of Infection** Serious bacterial, mycobacterial, fungal and viral infections have occurred *[see Adverse Reactions (6.1) in Full Prescribing Information]*. Delay starting therapy with Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines. *Tuberculosis* Tuberculosis infection has been reported in patients receiving Jakafi. Observe patients receiving Jakafi for signs and symptoms of active tuberculosis and manage promptly. Prior to initiating Jakafi, patients should be evaluated for tuberculosis risk factors, and those at higher risk should be tested for latent infection. Risk factors include, but are not limited to, prior residence in or travel to countries with a high prevalence of tuberculosis, close contact with a person with active tuberculosis, and a history of active or latent tuberculosis where an adequate course of treatment cannot be confirmed. For patients with evidence of active or latent tuberculosis, consult a physician with expertise in the treatment of tuberculosis before starting Jakafi. The decision to continue Jakafi during treatment of active tuberculosis should be based on the overall risk-benefit determination. *Progressive Multifocal Leukoencephalopathy* Progressive multifocal leukoencephalopathy (PML) has occurred with Jakafi treatment. If PML is suspected, stop Jakafi and evaluate. *Herpes Zoster* Advise patients about early signs and symptoms of herpes zoster and to seek treatment as early as possible if suspected. *Hepatitis B* Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking Jakafi. The effect of Jakafi on viral replication in patients with chronic HBV infection is unknown. Patients with chronic HBV infection should be treated and monitored according to clinical guidelines. **Symptom Exacerbation Following Interruption or Discontinuation of Treatment with Jakafi** Following discontinuation of Jakafi, symptoms from myeloproliferative neoplasms may return to pretreatment levels over a period of approximately one week. Some patients with MF have experienced one or more of the following adverse events after discontinuing Jakafi: fever, respiratory distress, hypotension, DIC, or multi-organ failure. If one or more of these occur after discontinuation of, or while tapering the dose of Jakafi, evaluate for and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi therapy without consulting their physician. When discontinuing or interrupting therapy with Jakafi for reasons other than thrombocytopenia or neutropenia *[see Dosage and Administration (2.7) in Full Prescribing Information]*, consider tapering the dose of Jakafi gradually rather than discontinuing abruptly. **Non-Melanoma Skin Cancer (NMSC)** Non-melanoma skin cancers including basal cell, squamous cell, and Merkel cell carcinoma have occurred in patients treated with Jakafi. Perform periodic skin examinations. **Lipid Elevations** Treatment with Jakafi has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides *[see Adverse Reactions (6.1) in Full Prescribing Information]*. The effect of these lipid parameter elevations on cardiovascular morbidity and mortality has not been determined in patients treated with Jakafi. Assess lipid parameters approximately 8-12 weeks following initiation of Jakafi therapy. Monitor and treat according to clinical guidelines for the management of hyperlipidemia. **Major Adverse Cardiovascular Events (MACE)** Another JAK-inhibitor has increased the risk of MACE, including cardiovascular death, myocardial infarction, and stroke (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur. **Thrombosis** Another JAK-inhibitor has increased the risk of thrombosis, including deep venous thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. In patients with MF and PV treated with Jakafi in clinical trials, the rates of thromboembolic events were similar in Jakafi and control treated patients. Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately. **Secondary Malignancies** Another JAK-inhibitor has increased the risk of lymphoma and other malignancies excluding NMSC (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi, particularly in patients with a known secondary malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers. **ADVERSE REACTIONS** The following clinically significant adverse reactions are discussed in greater detail in other sections of the labeling: • Thrombocytopenia, Anemia and Neutropenia *[see Warnings and Precautions (5.1) in Full Prescribing Information]* • Risk of Infection *[see Warnings and Precautions (5.2) in Full Prescribing Information]* • Symptom Exacerbation Following Interruption or Discontinuation of Treatment with Jakafi *[see Warnings and Precautions (5.3) in Full Prescribing Information ]* • Non-Melanoma Skin Cancer *[see Warnings and Precautions (5.4) in Full Prescribing Information]* • Lipid Elevations *[see Warnings and Precautions (5.5) in Full Prescribing Information]* • Major Adverse Cardiovascular Events (MACE) *[see Warnings and Precautions (5.6) in Full Prescribing Information]* • Thrombosis *[see Warnings and Precautions (5.7) in Full Prescribing Information]* • Secondary Malignancies *[see Warnings and Precautions (5.8) in Full Prescribing Information]*. **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.

Myelofibrosis The safety of Jakafi was assessed in 617 patients in six clinical studies with a median duration of follow-up of 10.9 months, including 301 patients with MF in two Phase 3 studies. In these two Phase 3 studies, patients had a median duration of exposure to Jakafi of 9.5 months (range 0.5 to 17 months), with 89% of patients treated for more than 6 months and 25% treated for more than 12 months. One hundred and eleven (111) patients started treatment at 15 mg twice daily and 190 patients started at 20 mg twice daily. In patients starting treatment with 15 mg twice daily (pretreatment platelet counts of 100 to 200 $\times 10^9$/L) and 20 mg twice daily (pretreatment platelet counts greater than 200 $\times 10^9$/L), 65% and 25% of patients, respectively, required a dose reduction below the starting dose within the first 8 weeks of therapy. In a double-blind, randomized, placebo-controlled study of Jakafi, among the 155 patients treated with Jakafi, the most frequent adverse reactions were thrombocytopenia and anemia *[see Table 2]*. Thrombocytopenia, anemia and neutropenia are dose-related effects. The three most frequent nonhematologic adverse reactions were bruising, dizziness and headache *[see Table 1]*. Discontinuation for adverse events, regardless of causality, was observed in 11% of patients treated with Jakafi and 11% of patients treated with placebo. Table 1 presents the most common nonhematologic adverse reactions occurring in patients who received Jakafi in the double-blind, placebo-controlled study during randomized treatment.

**Table 1: Myelofibrosis: Nonhematologic Adverse Reactions Occurring in Patients on Jakafi in the Double-blind, Placebo-controlled Study During Randomized Treatment**

| | Jakafi (N=155) | | | Placebo (N=151) | | |
|---|---|---|---|---|---|---|
| **Adverse Reactions** | **All Grades[a] (%)** | **Grade 3 (%)** | **Grade 4 (%)** | **All Grades (%)** | **Grade 3 (%)** | **Grade 4 (%)** |
| Bruising[b] | 23 | < 1 | 0 | 15 | 0 | 0 |
| Dizziness[c] | 18 | < 1 | 0 | 7 | 0 | 0 |
| Headache | 15 | 0 | 0 | 5 | 0 | 0 |
| Urinary Tract Infections[d] | 9 | 0 | 0 | 5 | < 1 | < 1 |
| Weight Gain[e] | 7 | < 1 | 0 | 1 | < 1 | 0 |
| Flatulence | 5 | 0 | 0 | < 1 | 0 | 0 |
| Herpes Zoster[f] | 2 | 0 | 0 | < 1 | 0 | 0 |

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0
[b] includes contusion, ecchymosis, hematoma, injection site hematoma, periorbital hematoma, vessel puncture site hematoma, increased tendency to bruise, petechiae, purpura
[c] includes dizziness, postural dizziness, vertigo, balance disorder, Meniere's Disease, labyrinthitis
[d] includes urinary tract infection, cystitis, urosepsis, urinary tract infection bacterial, kidney infection, pyuria, bacteria urine, bacteria urine identified, nitrite urine present
[e] includes weight increased, abnormal weight gain
[f] includes herpes zoster and post-herpetic neuralgia

**Description of Selected Adverse Reactions: Anemia** In the two Phase 3 clinical studies, median time to onset of first CTCAE Grade 2 or higher anemia was approximately 6 weeks. One patient (< 1%) discontinued treatment because of anemia. In patients receiving Jakafi, mean decreases in hemoglobin reached a nadir of approximately 1.5 to 2.0 g/dL below baseline after 8 to 12 weeks of therapy and then gradually recovered to reach a new steady state that was approximately 1.0 g/dL below baseline. This pattern was observed in patients regardless of whether they had received transfusions during therapy. In the randomized, placebo-controlled study, 60% of patients treated with Jakafi and 38% of patients receiving placebo received red blood cell transfusions during randomized treatment. Among transfused patients, the median number of units transfused per month was 1.2 in patients treated with Jakafi and 1.7 in placebo treated patients. **Thrombocytopenia** In the two Phase 3 clinical studies, in patients who developed Grade 3 or 4 thrombocytopenia, the median time to onset was approximately 8 weeks. Thrombocytopenia was generally reversible with dose reduction or dose interruption. The median time to recovery of platelet counts above $50 \times 10^9$/L was 14 days. Platelet transfusions were administered to 5% of patients receiving Jakafi and to 4% of patients receiving control regimens. Discontinuation

of treatment because of thrombocytopenia occurred in < 1% of patients receiving Jakafi and < 1% of patients receiving control regimens. Patients with a platelet count of 100 × $10^9$/L to 200 × $10^9$/L before starting Jakafi had a higher frequency of Grade 3 or 4 thrombocytopenia compared to patients with a platelet count greater than 200 × $10^9$/L (17% versus 7%). **Neutropenia** In the two Phase 3 clinical studies, 1% of patients reduced or stopped Jakafi because of neutropenia. Table 2 provides the frequency and severity of clinical hematology abnormalities reported for patients receiving treatment with Jakafi or placebo in the placebo-controlled study.

**Table 2: Myelofibrosis: Worst Hematology Laboratory Abnormalities in the Placebo-Controlled Study[a]**

| | Jakafi (N=155) | | | Placebo (N=151) | | |
|---|---|---|---|---|---|---|
| **Laboratory Parameter** | **All Grades[b] (%)** | **Grade 3 (%)** | **Grade 4 (%)** | **All Grades (%)** | **Grade 3 (%)** | **Grade 4 (%)** |
| Thrombocytopenia | 70 | 9 | 4 | 31 | 1 | 0 |
| Anemia | 96 | 34 | 11 | 87 | 16 | 3 |
| Neutropenia | 19 | 5 | 2 | 4 | < 1 | 1 |

[a] Presented values are worst Grade values regardless of baseline
[b] National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0

**Additional Data from the Placebo-Controlled Study**
• 25% of patients treated with Jakafi and 7% of patients treated with placebo developed newly occurring or worsening Grade 1 abnormalities in alanine transaminase (ALT). The incidence of greater than or equal to Grade 2 elevations was 2% for Jakafi with 1% Grade 3 and no Grade 4 ALT elevations. • 17% of patients treated with Jakafi and 6% of patients treated with placebo developed newly occurring or worsening Grade 1 abnormalities in aspartate transaminase (AST). The incidence of Grade 2 AST elevations was < 1% for Jakafi with no Grade 3 or 4 AST elevations. • 17% of patients treated with Jakafi and < 1% of patients treated with placebo developed newly occurring or worsening Grade 1 elevations in cholesterol. The incidence of Grade 2 cholesterol elevations was < 1% for Jakafi with no Grade 3 or 4 cholesterol elevations. Polycythemia Vera In a randomized, open-label, active-controlled study, 110 patients with PV resistant to or intolerant of hydroxyurea received Jakafi and 111 patients received best available therapy *[see Clinical Studies (14.2) in Full Prescribing Information]*. The most frequent adverse reaction was anemia. Discontinuation for adverse events, regardless of causality, was observed in 4% of patients treated with Jakafi. Table 3 presents the most frequent nonhematologic adverse reactions occurring up to Week 32.

**Table 3: Polycythemia Vera: Nonhematologic Adverse Reactions Occurring in ≥ 5% of Patients on Jakafi in the Open-Label, Active-controlled Study up to Week 32 of Randomized Treatment**

| | Jakafi (N=110) | | Best Available Therapy (N=111) | |
|---|---|---|---|---|
| **Adverse Reactions** | **All Grades[a] (%)** | **Grade 3-4 (%)** | **All Grades (%)** | **Grade 3-4 (%)** |
| Diarrhea | 15 | 0 | 7 | < 1 |
| Dizziness[b] | 15 | 0 | 13 | 0 |
| Dyspnea[c] | 13 | 3 | 4 | 0 |
| Muscle Spasms | 12 | < 1 | 5 | 0 |
| Constipation | 8 | 0 | 3 | 0 |
| Herpes Zoster[d] | 6 | < 1 | 0 | 0 |
| Nausea | 6 | 0 | 4 | 0 |
| Weight Gain[e] | 6 | 0 | < 1 | 0 |
| Urinary Tract Infections[f] | 6 | 0 | 3 | 0 |
| Hypertension | 5 | < 1 | 3 | < 1 |

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0
[b] includes dizziness and vertigo
[c] includes dyspnea and dyspnea exertional
[d] includes herpes zoster and post-herpetic neuralgia
[e] includes weight increased and abnormal weight gain
[f] includes urinary tract infection and cystitis

Clinically relevant laboratory abnormalities are shown in Table 4.

**Table 4: Polycythemia Vera: Selected Laboratory Abnormalities in the Open-Label, Active-controlled Study up to Week 32 of Randomized Treatment[a]**

| | Jakafi (N=110) | | | Best Available Therapy (N=111) | | |
|---|---|---|---|---|---|---|
| **Laboratory Parameter** | **All Grades[b] (%)** | **Grade 3 (%)** | **Grade 4 (%)** | **All Grades (%)** | **Grade 3 (%)** | **Grade 4 (%)** |
| **Hematology** | | | | | | |
| Anemia | 72 | < 1 | < 1 | 58 | 0 | 0 |
| Thrombocytopenia | 27 | 5 | < 1 | 24 | 3 | < 1 |
| Neutropenia | 3 | 0 | < 1 | 10 | < 1 | 0 |
| **Chemistry** | | | | | | |
| Hypercholesterolemia | 35 | 0 | 0 | 8 | 0 | 0 |
| Elevated ALT | 25 | < 1 | 0 | 16 | 0 | 0 |
| Elevated AST | 23 | 0 | 0 | 23 | < 1 | 0 |
| Hypertriglyceridemia | 15 | 0 | 0 | 13 | 0 | 0 |

[a] Presented values are worst Grade values regardless of baseline
[b] National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0

Acute Graft-Versus-Host Disease In a single-arm, open-label study, 71 adults (ages 18-73 years) were treated with Jakafi for aGVHD failing treatment with steroids with or without other immunosuppressive drugs *[see Clinical Studies (14.3) in Full Prescribing Information]*. The median duration of treatment with Jakafi was 46 days (range, 4-382 days). There were no fatal adverse reactions to Jakafi. An adverse reaction resulting in treatment discontinuation occurred in 31% of patients. The most common adverse reaction leading to treatment discontinuation was infection (10%). Table 5 shows the adverse reactions other than laboratory abnormalities.

**Table 5: Acute Graft-Versus-Host Disease: Nonhematologic Adverse Reactions Occurring in ≥ 15% of Patients in the Open-Label, Single-Cohort Study**

| | Jakafi (N=71) | |
|---|---|---|
| **Adverse Reactions[a]** | **All Grades[b] (%)** | **Grade 3-4 (%)** |
| Infections (pathogen not specified) | 55 | 41 |
| Edema | 51 | 13 |
| Hemorrhage | 49 | 20 |
| Fatigue | 37 | 14 |
| Bacterial infections | 32 | 28 |
| Dyspnea | 32 | 7 |
| Viral infections | 31 | 14 |
| Thrombosis | 25 | 11 |
| Diarrhea | 24 | 7 |
| Rash | 23 | 3 |
| Headache | 21 | 4 |
| Hypertension | 20 | 13 |
| Dizziness | 16 | 0 |

[a] Selected laboratory abnormalities are listed in Table 6 below
[b] National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 4.03

Selected laboratory abnormalities during treatment with Jakafi are shown in Table 6.

**Table 6: Acute Graft-Versus-Host Disease: Selected Laboratory Abnormalities Worsening from Baseline in the Open-Label, Single Cohort Study**

| | Jakafi (N=71) | |
|---|---|---|
| | Worst grade during treatment | |
| **Laboratory Parameter** | **All Grades[a] (%)** | **Grade 3-4 (%)** |
| **Hematology** | | |
| Anemia | 75 | 45 |
| Thrombocytopenia | 75 | 61 |
| Neutropenia | 58 | 40 |
| **Chemistry** | | |
| Elevated ALT | 48 | 8 |
| Elevated AST | 48 | 6 |
| Hypertriglyceridemia | 11 | 1 |

[a] National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03

Chronic Graft-Versus-Host Disease In a Phase 3, randomized, open-label, multi-center study, 165 patients were treated with Jakafi and 158 patients were treated with best available therapy for cGVHD failing treatment with steroids with or without other immunosuppressive drugs *[see Clinical Studies (14.4) in full Prescribing Information]*; sixty-five patients crossed over from best available therapy to treatment with Jakafi, for a total of 230 patients treated with Jakafi. The median duration of exposure to Jakafi for the study was 49.7 weeks (range, 0.7 to 144.9 weeks) in the Jakafi arm. One hundred and nine (47%) patients were on Jakafi for at least 1 year. There were five fatal adverse reactions to Jakafi, including 1 from toxic epidermal necrolysis and 4 from neutropenia, anemia and/or thrombocytopenia. An adverse reaction resulting in treatment discontinuation occurred in 18% of patients treated with Jakafi. An adverse reaction resulting in dose modification occurred in 27%, and an adverse reaction resulting in treatment interruption occurred in 23%. The most common hematologic adverse reactions (incidence > 35%) are anemia and thrombocytopenia. The most common nonhematologic adverse reactions (incidence ≥ 20%) are infections (pathogen not specified) and viral infection. Table 7 presents the most frequent nonlaboratory adverse reactions occurring up to Cycle 7 Day 1 of randomized treatment.

**Table 7: Chronic Graft-Versus-Host Disease: All-Grade (≥ 10%) and Grades 3-5 (≥ 3%) Nonlaboratory Adverse Reactions Occurring in Patients in the Open-Label, Active-controlled Study up to Cycle 7 Day 1 of Randomized Treatment**

| | Jakafi (N = 165) | | Best Available Therapy (N = 158) | |
|---|---|---|---|---|
| **Adverse Reactions[b]** | **All Grades[a] (%)** | **Grade ≥ 3 (%)** | **All Grades (%)** | **Grade ≥ 3 (%)** |
| **Infections and infestations** | | | | |
| Infections (pathogen not specified) | 45 | 15 | 44 | 16 |
| Viral infections | 28 | 5 | 23 | 5 |
| **Musculoskeletal and connective tissue disorders** | | | | |
| Musculoskeletal pain | 18 | 1 | 13 | 0 |
| **General disorders and administration site conditions** | | | | |
| Pyrexia | 16 | 2 | 9 | 1 |
| Fatigue | 13 | 1 | 10 | 2 |
| Edema | 10 | 1 | 12 | 1 |
| **Vascular disorders** | | | | |
| Hypertension | 16 | 5 | 13 | 7 |
| Hemorrhage | 12 | 2 | 15 | 2 |
| **Respiratory, thoracic and mediastinal disorders** | | | | |
| Cough | 13 | 0 | 8 | 0 |
| Dyspnea | 11 | 1 | 8 | 1 |
| **Gastrointestinal disorders** | | | | |
| Nausea | 12 | 0 | 13 | 2 |
| Diarrhea | 10 | 1 | 13 | 1 |

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 4.03
[b] Grouped terms that are composites of applicable adverse reaction terms.

Clinically relevant laboratory abnormalities are shown in Table 8.

**Table 8: Chronic Graft-Versus-Host Disease: Selected Laboratory Abnormalities in the Open-Label, Active-controlled Study up to Cycle 7 Day 1 of Randomized Treatment[a]**

| | Jakafi (N=165) | | Best Available Therapy (N=158) | |
|---|---|---|---|---|
| **Laboratory Test** | **All Grades[b] (%)** | **Grade ≥ 3 (%)** | **All Grades (%)** | **Grade ≥ 3 (%)** |
| **Hematology** | | | | |
| Anemia | 82 | 13 | 75 | 8 |
| Thrombocytopenia | 27 | 12 | 23 | 9 |
| Neutropenia | 58 | 20 | 54 | 17 |
| **Chemistry** | | | | |
| Hypercholesterolemia | 88 | 10 | 85 | 8 |
| Elevated AST | 65 | 5 | 54 | 6 |
| Elevated ALT | 73 | 11 | 71 | 16 |
| Gamma glutamyltransferase increased | 81 | 42 | 75 | 38 |
| Creatinine increased | 47 | 1 | 40 | 2 |
| Elevated lipase | 38 | 12 | 30 | 9 |
| Elevated amylase | 35 | 8 | 25 | 4 |

[a] Presented values are worst Grade values regardless of baseline
[b] National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03

**DRUG INTERACTIONS Fluconazole** Concomitant use of Jakafi with fluconazole increases ruxolitinib exposure *[see Clinical Pharmacology (12.3) in Full Prescribing Information]*, which may increase the risk of exposure-related adverse reactions. Avoid concomitant use of Jakafi with fluconazole doses of greater than 200 mg daily. Reduce the Jakafi dosage when used concomitantly with fluconazole doses of less than or equal to 200 mg *[see Dosage and Administration (2.5) in Full Prescribing Information]*. **Strong CYP3A4 Inhibitors** Concomitant use of Jakafi with strong CYP3A4 inhibitors increases ruxolitinib exposure *[see Clinical Pharmacology (12.3) in Full Prescribing Information]*, which may increase the risk of exposure-related adverse reactions. Reduce the Jakafi dosage when used concomitantly with strong CYP3A4 inhibitors except in patients with aGVHD or cGVHD *[see Dosage and Administration (2.5) in Full Prescribing Information]*. **Strong CYP3A4 Inducers** Concomitant use of Jakafi with strong CYP3A4 inducers may decrease ruxolitinib exposure *[see Clinical Pharmacology (12.3) in Full Prescribing Information]*, which may reduce efficacy of Jakafi. Monitor patients frequently and adjust the Jakafi dose based on safety and efficacy *[see Clinical Pharmacology (12.3) in Full Prescribing Information]*.

**USE IN SPECIFIC POPULATIONS Pregnancy: Risk Summary** When pregnant rats and rabbits were administered ruxolitinib during the period of organogenesis adverse developmental outcomes occurred at doses associated with maternal toxicity *(see Data)*. There are no studies with the use of Jakafi in pregnant women to inform drug-associated risks. The background risk of major birth defects and miscarriage for the indicated populations is unknown. Adverse outcomes in pregnancy occur regardless of the health of the mother or the use of medications. The background risk in the U.S. general population of major birth defects is 2% to 4% and miscarriage is 15% to 20% of clinically recognized pregnancies. **Data:** *Animal Data* Ruxolitinib was administered orally to pregnant rats or rabbits during the period of organogenesis, at doses of 15, 30 or 60 mg/kg/day in rats and 10, 30 or 60 mg/kg/day in rabbits. There were no treatment-related malformations. Adverse developmental outcomes, such as decreases of approximately 9% in fetal weights were noted in rats at the highest and maternally toxic dose of 60 mg/kg/day. This dose results in an exposure (AUC) that is approximately 2 times the clinical exposure at the maximum recommended dose of 25 mg twice daily. In rabbits, lower fetal weights of approximately 8% and increased late resorptions were noted at the highest and maternally toxic dose of 60 mg/kg/day. This dose is approximately 7% the clinical exposure at the maximum recommended dose. In a pre- and post-natal development study in rats, pregnant animals were dosed with ruxolitinib from implantation through lactation at doses up to 30 mg/kg/day. There were no drug-related adverse findings in pups for fertility indices or for maternal or embryofetal survival, growth and development parameters at the highest dose evaluated (34% the clinical exposure at the maximum recommended dose of 25 mg twice daily). **Lactation: Risk Summary** No data are available regarding the presence of ruxolitinib in human milk, the effects on the breast fed child, or the effects on milk production. Ruxolitinib and/or its metabolites were present in the milk of lactating rats *(see Data)*. Because many drugs are present in human milk and because of the potential for thrombocytopenia and anemia shown for Jakafi in human studies, discontinue breastfeeding during treatment with Jakafi and for two weeks after the final dose. **Data:** *Animal Data* Lactating rats were administered a single dose of [$^{14}$C]-labeled ruxolitinib (30 mg/kg) on postnatal Day 10, after which plasma and milk samples were collected for up to 24 hours. The AUC for total radioactivity in milk was approximately 13-fold the maternal plasma AUC. Additional analysis showed the presence of ruxolitinib and several of its metabolites in milk, all at levels higher than those in maternal plasma. **Pediatric Use** The safety and effectiveness of Jakafi for treatment of myelofibrosis or polycythemia vera in pediatric patients have not been established. The safety and effectiveness of Jakafi for treatment of steroid-refractory aGVHD has been established for treatment of children 12 years and older. Use of Jakafi in pediatric patients with steroid-refractory aGVHD is supported by evidence from adequate and well-controlled trials of Jakafi in adults *[see Clinical Studies (14.3) in Full Prescribing Information]* and additional pharmacokinetic and safety data in pediatric patients. The safety and effectiveness of Jakafi for treatment of steroid-refractory aGVHD has not been established in pediatric patients younger than 12 years old. The safety and effectiveness of Jakafi for treatment of cGVHD after failure of one or two lines of systemic therapy has been established for treatment of children 12 years and older. Use of Jakafi in pediatric patients with cGVHD after failure of one or two lines of systemic therapy is supported by evidence from adequate and well-controlled trials of Jakafi in adults and adolescents *[see Clinical Studies (14.3, 14.4) in Full Prescribing Information]* and additional pharmacokinetic and safety data in pediatric patients. The safety and effectiveness of Jakafi for treatment of cGVHD has not been established in pediatric patients younger than 12 years old. Jakafi was evaluated in a single-arm, dose-escalation study (NCT01164163) in 27 pediatric patients with relapsed or refractory solid tumors (Cohort A) and 20 with leukemias or myeloproliferative neoplasms (Cohort B). The patients had a median age of 14 years (range, 2 to 21 years) and included 18 children (age 2 to < 12 years), and 14 adolescents (age 12 to < 17 years). The dose levels tested were 15, 21, 29, 39, or 50 mg/m$^2$ twice daily in 28-day cycles with up to 6 patients per dose group. Overall, 38 (81%) patients were treated with no more than a single cycle of Jakafi, while 3, 1, 2, and 3 patients received 2, 3, 4, and 5 or more cycles, respectively. A protocol-defined maximal tolerated dose was not observed, but since few patients were treated for multiple cycles, tolerability with continued use was not assessed adequately to establish a recommended Phase 2 dose higher than the recommended dose for adults. The safety profile in children was similar to that seen in adults. *Juvenile Animal Toxicity Data* Administration of ruxolitinib to juvenile rats resulted in effects on growth and bone measures. When administered starting at postnatal day 7 (the equivalent of a human newborn) at doses of 1.5 to 75 mg/kg/day, evidence of fractures occurred at doses ≥ 30 mg/kg/day, and effects on body weight and other bone measures [e.g., bone mineral content, peripheral quantitative computed tomography, and x-ray analysis] occurred at doses ≥ 5 mg/kg/day. When administered starting at postnatal day 21 (the equivalent of a human 2-3 years of age) at doses of 5 to 60 mg/kg/day, effects on body weight and bone occurred at doses ≥ 15 mg/kg/day, which were considered adverse at 60 mg/kg/day. Males were more severely affected than females in all age groups, and effects were generally more severe when administration was initiated earlier in the postnatal period. These findings were observed at exposures that are at least 27% the clinical exposure at the maximum recommended dose of 25 mg twice daily. **Geriatric Use** Of the total number of patients with MF in clinical studies with Jakafi, 52% were 65 years and older, while 15% were 75 years and older. No overall differences in safety or effectiveness of Jakafi were observed between these patients and younger patients. Clinical studies of Jakafi in patients with aGVHD did not include sufficient numbers of subjects age 65 and over to determine whether they respond differently from younger subjects. Of the total number of patients with cGVHD treated with Jakafi in clinical trials, 11% were 65 years and older. No overall differences in safety or effectiveness of Jakafi were observed between these patients and younger patients. **Renal Impairment** Total exposure of ruxolitinib and its active metabolites increased with moderate (CLcr 30 to 59 mL/min) and severe (CLcr 15 to 29 mL/min) renal impairment, and ESRD (CLcr less than 15 mL/min) on dialysis *[see Clinical Pharmacology (12.3) in Full Prescribing Information]*. Modify Jakafi dosage as recommended *[see Dosage and Administration (2.6) in full Prescribing Information]*. **Hepatic Impairment** Exposure of ruxolitinib increased with mild (Child-Pugh A), moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. Reduce Jakafi dosage as recommended in patients with MF or PV with hepatic impairment *[see Dosage and Administration (2.6) in full Prescribing Information]*. Reduce Jakafi dosage as recommended for patients with Stage 4 liver aGVHD. Monitor blood counts more frequently for toxicity and modify the Jakafi dosage for adverse reactions if they occur for patients with Score 3 liver cGVHD *[see Dosage and Administration (2.6) and Clinical Pharmacology (12.3) in full Prescribing Information]*. **OVERDOSAGE** There is no known antidote for overdoses with Jakafi. Single doses up to 200 mg have been given with acceptable acute tolerability. Higher than recommended repeat doses are associated with increased myelosuppression including leukopenia, anemia and thrombocytopenia. Appropriate supportive treatment should be given. Hemodialysis is not expected to enhance the elimination of Jakafi.


Revised: September 2021 PLR-JAK-00054

# IN THIS ISSUE

## FEATURES



## SPOTLIGHTS



## DEPARTMENTS



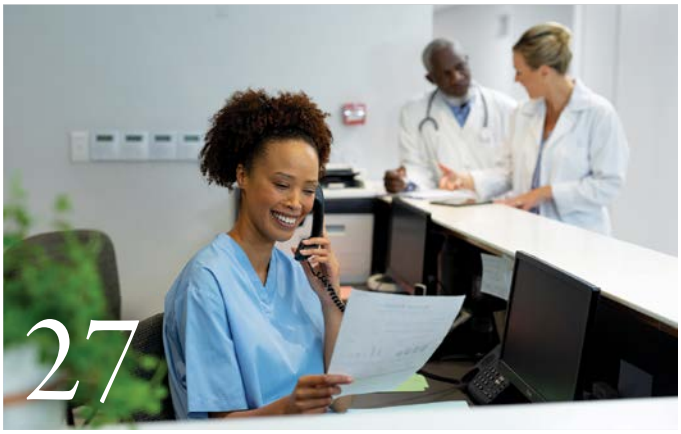
We welcome your feedback, article suggestions and photos (high resolution please).

Email to FCSCommunications@FLCancer.com

**On the cover:** Siblings Marshe and Gregory Ford and Zaza Wright

Photography by Robyn Barkley Photography




PHOTOS BY OCTAVIO JONES (10), ROBYN BARKLEY PHOTOGRAPHY (14) AND WAVEBREAKMEDIA (26)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### NATHAN H. WALCKER, CHIEF EXECUTIVE OFFICER

"Little Things," our newest brand campaign, captures the essence of the unique connections we build with our patients at every step of their cancer journey. It's truly authentic, showcasing the expert care and compassion that FCS team members provide paired with innovation and state-of-the-art technology — the big things — that enable patients to spend more time on the little things — enjoying life's meaningful moments.

You'll find more touching stories in this issue.

Jacqueline Ambrose shares how she honors the memory of three family members lost to cancer in her professional role as FCS Associate General Counsel.

Gregory and Marshe Ford and Zaza Wright are siblings who have chosen to build their careers at FCS and strive to be the best they can be for our patients.

And while our team members touch lives in clinics across the state, two FCS nurses were recently called to service 30,000 feet above ground, to provide life-saving treatment to a fellow airline passenger.

It would be impossible to achieve what we do if we did not have the right individuals in place. As the final months of the year come into focus, seeing all that we have accomplished together makes me even more enthusiastic for all that is before us. Thank you all for your efforts that matter so much to those who entrust their care to FCS.

### MICHAEL DIAZ, MD, PRESIDENT & MANAGING PHYSICIAN

Every day, our physicians, team members and patients are contributing to exciting innovations in cancer diagnosis and treatment. Over the summer, 18 Florida Cancer Specialists physicians presented the findings of more than 30 clinical trials conducted at FCS with their peers at the prestigious ASCO Annual Meeting. FCS is in the spotlight regularly at professional gatherings, sharing research outcomes that are evolving cancer care globally and providing new hope for patients.

The opening of our new clinic in Kissimmee was a significant step forward to provide access to world-class cancer care in a new Central Florida market — home to half a million permanent residents and growing at a rate of about 4% each year. Similarly, on the west coast, our new patient-centric location in Zephyrhills Green Slope has further expanded access to residents in Pasco County.

We are delighted to welcome several new Board-certified medical oncologists to our practice. Each has exceptional credentials and shares our commitment to ensuring that patients receive the most advanced and personalized treatments.

As one ever-expanding team, with one mission, our physicians and team members continue to give their very best so that our patients experience the best outcomes possible. Thank you, for all that you do.


JACQUELINE AMBROSE

# A Litigator's Family Legacy

## Jacqueline Ambrose honors her loved ones by helping others in her role at FCS

**BY PAIGE AIGRET // PHOTOS BY OCTAVIO JONES**

Although she's a year into her position as Associate General Counsel with Florida Cancer Specialists & Research Institute (FCS), Jacqueline Ambrose has a much longer history with the practice. After losing her mother, father and sister all to different forms of cancer, Jacqueline wanted nothing more than to help serve the physicians and patients at FCS.

With an education in political science and law and experience in medical law practice litigation, Jacqueline was certainly qualified, but there were greater influences in her decision.

"For a lot of reasons, choosing to work for FCS is personal," said Jacqueline. "It's sort of a legacy for me. While my story is incredibly heartbreaking … there were so many good things that came out of it."

And she's found catharsis in being able to share her story.

Her mom, Rose Marie Ambrose, was first diagnosed with breast cancer in 2003, setting the family on a long, traumatic journey with the disease.

"It was disbelief because my mom was this firecracker of a human being. Nothing could keep her down," said Jacqueline.

A fighter, she was. And after some rounds of treatment, she healed. But despite being in remission for six years, her cancer returned in 2009.

"We all rallied around my mom and how strong she was," said Jacqueline.

The days grew more taxing and Rose was in need of treatment closer to home. Jacqueline had come to know Chrissy Wenk, as they were frequently aligned in their work at the time and had become friends. As they grew closer, Jacqueline shared her family's story and Chrissy suggested that they make an appointment with her husband, FCS Medical Oncologist Dr. David Wenk.

"He and my mom just got each other from day one," said Jacqueline. "The amount that Dave really cared about my mom became evident, not just in the way he treated her and in the way their patient-physician relationship developed

"My mom always said, 'I don't want my symbol to be a pink ribbon. I am more than my disease,' and that's how she lived. She refused to let it define her, which kind of made us not allowed to let it define her either."

through mom's treatment, but in the way he treated my whole family."

The family continued to focus on strength over fear, and Rose healed a second time. But her battle continued as she came out of remission once again.

"The third time hit like a ton of bricks," Jacqueline recalled.

When her sister, Erica Hoffman, was diagnosed with colorectal cancer, the family was shaken once again. Still, they found moments of grace. One of them being that Rose and Erica were able to share their hardships.

"My mom and my sister, in the last years of their lives, were able to connect on this incredibly meaningful level to support each other and to really understand each other in a way that no one else could."

Still, the family did everything they could to maintain normalcy in their daily lives.

"My mom always said, 'I don't want my symbol to be a pink ribbon. I am more than my disease,' and that's how she lived. She refused to let it define her, which kind of made us not allowed to let it define her either," Jacqueline said with a laugh.

Sadly, Rose passed in May 2018.

The family became focused on Erica's health, but it wasn't long before they received another cancer blow, as their father, Mike Ambrose, was diagnosed with pancreatic cancer just weeks after his wife's celebration of life.

Still reeling from losing her mother, Jacqueline recognized, "I kind of had to put that on a shelf and deal with the horrors in front of me.

"When he was diagnosed, I think we all kind of lost our spirit a bit," she expressed. They were losing faith.

Jacqueline with her daughter, Lillian, and father Mike.

"In my dad, we really hadn't understood the symptoms, because, I will tell you, any widower of 40-plus years will have weight loss and stomach pain," said Jacqueline.

But they found stability in the support and care at FCS, as Dr. Wenk went on to be Mike's physician and would offer support and advice for Erica as well.

"To have that in a physician, especially a busy oncology group, it was a palpable difference," said Jacqueline. "He was really just incredibly caring, empathetic and there for my family."

When they first caught Mike's cancer, it was still operable. But it wasn't long before it returned in the aggressive way that pancreatic cancer is known for.

"Thankfully, Dr. Wenk prepared me for that as best he could," said Jacqueline.

Meanwhile, her sister began to fail, too.

"I did my very best to split time between a failing father, and grandfather to my young children, and spending time with my sister," said Jacqueline. "It was just every ounce of strength I had to try to keep it all together."

Visiting her sister in those final months, they spent a lot of time just lying in bed together. "I don't think we had slept in the same bed since we were kids, but we just wanted to spend the time."

When her sister passed away in July 2019, it took an additional toll, especially for Jacqueline's father, already declining in health. "I would have spared him that if I at all could," she said.

Mike passed just five months after losing Erica.

"Honestly, July to December of '19 is a blur," said Jacqueline, who was diagnosed with complicated grief, a condition that occurs in only 7% of bereaved people, as well as PTSD, anxiety and depression.

"As we sit here now in 2022, I'm just beginning to be able to process the magnitude of loss," she said.

"Sometimes when I think of them … it's to laugh, or it's to tell a funny story, or to smile or play a game with my girls and tell them that I learned it from their Pop-Pop. It will never not be incredibly painful, but … I am finally to the point where there can be this joyful remembrance."

She focuses now on keeping her family's memory alive for her two daughters, Lillian and Filomena, who were both quite young amid the waves of loss. She shares stories and they look at photos. As a mother, looking forward has become important to Jacqueline.

"The process of building new traditions has been a big part of my life. I'm doing everything in my power to create for my girls that nest and that feeling of love and security surrounding them that I had when I was a kid."

> "I'm really proud of the direction FCS is going and the company itself. Our values, our mission; it aligns with who I am as a person. It's really just been a wonderful fit for me. It's a job, but it completely has my heart."

Jacqueline remains the hardworking, selfless lawyer she's always been. And she's doing that with the very company that helped guide her and her family through their own journey.

"I'm really proud of the direction FCS is going and the company itself," said Jacqueline. "Our values, our mission; it aligns with who I am as a person. It's really just been a wonderful fit for me.

"It's a job, but it completely has my heart."

*MARSHE, ZAZA AND GREGORY*

# It Runs in the Family

## How three siblings found their passion working with FCS

**BY EVGENIYA STETSENKO**
**PHOTOS BY ROBYN BARKLEY PHOTOGRAPHY**

"Families are the compass that guides us. They are the inspiration to reach great heights and our comfort when we occasionally falter." — Brad Henry

Siblings Gregory and Marshe Ford and Zaza Wright have each discovered their passion for helping others during challenging times in their respective roles at Florida Cancer Specialists & Research Institute (FCS).

Marshe Ford, hired in 2017, works in the Central Scheduling department at the FCS Fort Myers Cancer Center. The workload was challenging at first, but she quickly found she was making a difference in the lives of patients through diligently scheduling appointments and always following up.

"Some test results are good, some are not, but I love my job so much because I know I can be helpful to people during this trying period of their lives," Marshe said.

In her five years with FCS, she has learned a lot about the care provided to patients and has mastered her communication and time management skills. Today, 11 physicians are practicing out of the Fort Myers Cancer Center. On average, 950 patients come through its doors each week, and at the heart of it all is Marshe.

## A FAMILY THAT SHINES AT FCS

### GREGORY FORD
***FCS Estero Clinic, Bonita Springs***

*Trafficking approximately 400 patients per week*

"Greg is truly a stellar asset to our clinic. His compassion for patients is unmatched, and he consistently goes above and beyond to help his team and physicians. Greg is a ray of sunshine in our clinic, and his contagious positivity really shines through to our patients, even in their most difficult times. It is an honor to have gotten to know Greg and his sisters through our time together at FCS. I know with their drive and dedication to providing outstanding patient care, they will all go far!" *— Ashlee Hickox, Estero Office Manager*

### MARSHE FORD
***FCS GLO Clinic, Fort Myers***

*Trafficking approximately 950 patients per week*

"Marshe is an intricate part of our FCS family. She is the familiar face our physicians and patients seek when scheduling their life-changing scans. She's the energetic, comedic co-worker that we all love to share the day with. She's there through each moment of hope, fear and happiness. Marshe is the essence of hometown care." *— Audrey Allen, GLO Office Manager*

### ZAZA WRIGHT
***FCS NPW Clinic, Naples***

*Trafficking approximately 800 patients per week*

"Zaza performs an outstanding job assisting patients at the front desk, she greets our patients in a way that makes them feel at home and she goes the extra mile when providing patients with all the necessary details for their upcoming appointments. Consistently, since her first day on the job, she has demonstrated such a positive attitude and has become a role model for her co-workers." *— Kiara Salcedo, NPW Interim Office Manager*

Gregory Ford joined FCS about one month after Marshe was hired. He started working in billing, then moved to collections and later accepted a position as a Patient Services Specialist at the FCS Estero clinic.

"I love my position and I love working at FCS because we are offered many opportunities to extend ourselves and grow," said Gregory.

Zaza has been working as an administrative specialist at FCS Naples West for one year. Her own experience of losing her grandmother to cancer has given purpose to helping others while they are going through a very challenging time in life. She has quickly learned the necessary medical terminology and scheduling procedures and enjoys supporting patients and the clinical staff.

While each of the siblings work in different roles and different locations, as a team they remain focused on the same compassionate goal of selfless care. Bettering themselves is also a common focus among the three, and FCS has been supportive of them achieving their personal goals.

Beyond her full-time role at FCS, Marshe is also a full-time student. She recently graduated with an associate degree in paralegal studies and plans to go to college to study law.

"I love my position and I love working at FCS because we are offered many opportunities to extend ourselves and grow."

Zaza is working on her nursing degree, thanks to support from FCS, who not only works with her schedule to make time for school, but also offers tuition reimbursement to qualified team members.

Among the many things Gregory has gained from working at FCS, his greatest source of inspiration comes from patients who have taught him to soak up all of life's splendors. While Gregory has been able to advance his career at FCS, he is also a singer and artist, and loves cooking and getting together with friends and family on his days off.

For Gregory, Marshe and Zaza, working at FCS has been one of the best experiences in their careers. They each love their roles, acknowledging that while it can sometimes be challenging and emotional, it is also very fulfilling and rewarding.

The three talk together often and find a little family time is all they need to recharge so they can be the best they can be at caring for their patients.

Working with families of cancer takes strength and perseverance. It often takes a village — or sometimes, a family.

# ASCO Recap

## FCS presence is notable at 2022 Annual Meeting

The American Society of Clinical Oncology (ASCO), which represents more than 45,000 oncology professionals, held its 2022 Annual Meeting June 3–6 in Chicago, Illinois. Professionals from across the country came together in person, for the first time in two years, to discuss and learn about advanced treatments, research and innovations in oncology care.

Several of the clinical trials presented were conducted by Florida Cancer Specialists & Research Institute (FCS) physicians. In fact, FCS has offered more patients access to clinical trials than any other private oncology practice in Florida. In the last five years, a majority of new cancer drugs approved to be used in the U.S. came from studies and clinical trials performed with FCS participation.

"It makes me incredibly proud, knowing that our patients have access to the most cutting-edge oncology therapies and treatments" said FCS President and Managing Physician Michael Diaz, MD. "Our ability to provide such advanced levels of care in a community-based setting is a large contributing factor to the success we see in our research — being able to treat patients close to home."

FCS Director of Drug Development Manish R. Patel, MD, noted the importance of FCS' presence and platform at the ASCO event.

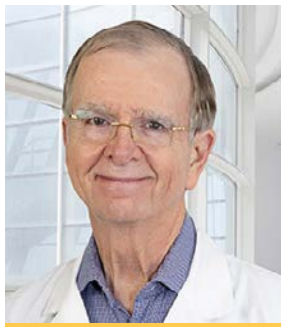
"Having the majority of newly approved oncology drugs and therapies in the United States originate from clinical trials conducted by FCS physicians, it is imperative that we share these advances with our peers so that we can continue to evolve cancer care," said Dr. Patel.

FCS physicians had the opportunity to present outcomes from 33 clinical trials conducted at FCS locations.

FCS Chief Executive Officer Nathan H. Walcker recognized the hard work of FCS physicians, stating, "Our physicians continue to be leaders in the oncology community, spearheading innovative approaches to cancer care on a global scale."

"Their efforts, both in our clinics and in the research presented at ASCO, speak volumes to the high-level patient care we provide at FCS and the entire oncology ecosystem," Walcker said.

**Manish R. Patel, MD**
FCS Director of Drug Development



**Lowell L. Hart, MD, FACP**
FCS Scientific Director of Clinical Research

**Shekeab Jauhari, MD**
FCS Associate Director of Drug Development

**Cesar Augusto Perez, MD**

**Lucio N. Gordan, MD**
FCS Chief Medical Officer of Therapeutics and Analytics

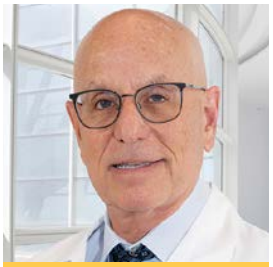
**Judy S. Wang, MD**
FCS Associate Director of Drug Development

Anjan J. Patel, MD

Matthew A. Fink, MD

Faithlore Gardner, MD

Elizabeth Guancial, MD



William N. Harwin, MD

Maen Hussein, MD

Joseph R. Mace, MD

James A. Reeves Jr., MD

David D. Wright, MD

Daniel L. Spitz, MD, FACP

**FCS presenters at the 2022 ASCO Annual Meeting included:**

- FCS Scientific Director of Clinical Research **Lowell L. Hart, MD, FACP**, who first-authored a poster discussion for a study on metastatic breast cancer and also co-authored a second poster presentation for extensive-stage small cell lung cancer.
- FCS Associate Director of Drug Development **Shekeab Jauhari, MD**, lead author for a poster presentation of an immunotherapy-based study for solid tumors and co-author for a Phase 1 study for advanced renal cell carcinoma and ovarian tumors, presented orally. **Dr. Jauhari retired from FCS in July 2022.*
- FCS Director of Drug Development **Manish R. Patel, MD**, lead author for a Phase 2 study poster discussion on advanced gynecologic malignancies, co-author of five additional Phase 1 trials in poster and oral presentations and one published study for non-small cell lung cancer.
- **Cesar Augusto Perez, MD**, lead author for a poster presentation of a first-in-human study for breast cancer and co-author of five poster presentations covering trials for molecularly targeted agents, melanoma and skin cancer, and head and neck cancer.
- FCS Chief Medical Officer of Therapeutics and Analytics **Lucio N. Gordan, MD**, lead author for a publication covering community oncology biomarker testing rates for non-small cell metastatic lung cancer alongside co-authors **Anjan J. Patel, MD**, and **Matthew A. Fink, MD**. Dr. Gordan also co-authored two studies on care delivery for lung cancer patients featured at the conference.

**Among other FCS presentations were a number of FCS physician investigators, including:**

- **Faithlore Gardner, MD** — hematologic malignancies
- **Elizabeth Guancial, MD** — molecularly targeted agents for metastatic solid tumors and urothelial carcinoma
- **William N. Harwin, MD** — lymphoma
- **Maen Hussein, MD** — lung cancer
- **Joseph R. Mace, MD** — plasma cell dyscrasia
- **James A. Reeves Jr., MD** — melanoma and skin cancer
- FCS Associate Director of Drug Development **Judy S. Wang, MD** — immunotherapy
- **David D. Wright, MD** — breast cancer

**The following FCS physician investigators presented research results during oral presentations:**

- **Daniel L. Spitz, MD, FACP** — molecular based treatment for endometrial cancer
- **Judy S. Wang, MD** — immunotherapy

*OUR INSPIRATION*

# Little Things Power Big Outcomes for Patients and Our Team

Our big breakthroughs in community oncology mean that patients across Florida can enjoy more of the little moments that make life special. Capturing this powerful insight is the core of our newest brand campaign, "Little Things." By showcasing Florida Cancer Specialists' unique benefits, we build connections with potential patients. And by highlighting our commitment to compassionate, comprehensive care, we nurture relationships with our current patients.

Launched in August, this campaign has been featured across TV, social media, print, outdoor billboards and digital banners. These platforms work together to raise brand awareness and push prospective patients to a landing page that acts as a central hub for our "Little Things" messaging. The campaign captures our position as a brand leader in both quality and expertise, focusing on how our patients have access to advanced care near their homes, friends and families, every step of the way.

> This campaign captures the little moments of joy that FCS patients live for.

Across a variety of media, this campaign captures the little moments of joy that FCS patients live for. Moving past the shock and worry of a diagnosis to a place of acceptance and resilience, we hope to inspire newly diagnosed patients, or those struggling to choose a cancer treatment provider, to take the necessary steps forward with us.

Viewers of the TV campaign get an inside look at our labs, facilities and technologies as we share how top-ranked experts provide the most advanced, personalized treatment based on patients' unique genes. Filmed locally at an FCS clinic location in Sarasota, the campaign sparked internal interest and excitement. Team members across a range of departments were able to show off their skills behind the scenes and in front of the camera.

While this work puts the spotlight on patients and their needs, we were, and continue to be, inspired by you. Your stories of care, expertise and compassion helped guide us. Every member of the FCS team plays a vital role in ensuring that our patients have more of the little things that matter most. We hope this work helps audiences remember that life can continue, even after a cancer diagnosis.

*To learn more about the Little Things campaign, visit FLCancer.com/littlethings.*

PHOTOS BY NORTONRSX AND PROSTOCK-STUDIO / ISTOCK / GETTY IMAGES PLUS

# Close to patients.
## Closer to what matters most.

From decoding DNA for genetic screening to connecting patients to leading clinical trial research organizations, we are delivering the most advanced innovations to more communities across Florida. By enabling patients to stay close to friends, family and their homes, we give them more of the time they need with the people that they love.

FLORIDA CANCER SPECIALISTS
& Research Institute

FLCancer.com/LittleThings

*EMPLOYEE SPOTLIGHT*

# Heroes on Land and in the Air

## Two off-duty FCS nurses save life on flight

**BY PAIGE AIGRET**



**Becton J. Roddenberry, BSN, RN, OCN, CEN, EMT-P**
Lead Nurse,
FCS Tallahassee Cancer Center



**Angella Campbell, RN, OCN**
FCS Orlando Orange

Becton Roddenberry and Angella Campbell are both registered nurses with Florida Cancer Specialists & Research Institute (FCS). While treating patients is hardly new to them, they didn't expect to be putting their experience to work while flying more than 30,000 feet in the air.

Roddenberry and Campbell were traveling home to Florida after having attended the 47th annual Oncology Nursing Society Congress, held in Anaheim, California. Just as they had settled into their American Airlines flight to layover in Dallas, Texas, something went awry.

A call for medical attention came, as a flight attendant made an overhead announcement asking if any medical professionals were on board.

"I guess adrenaline had taken over because I don't recall hearing the announcement," Campbell said.

She hadn't needed the announcement to know help was needed. She'd heard a woman in a nearby seat cry out, "oh, god!" as she was trying to shake an incapacitated passenger awake and keep her from falling out of her seat.

"When I realized that the young lady was unconscious, my first thought was I needed to do something and my second thought was to locate Becton," said Campbell.

Roddenberry echoed Campbell's sentiment, saying, "I don't think there was any initial thought, it's more of a reflex." All that came to his mind was getting the passenger stabilized.

The passenger, a young woman, was in what Campbell noted to be a "catatonic state." She had fainted and was extremely lethargic and pale. Immediately after seeing the situation at hand, Roddenberry and Campbell locked eyes, both ready to respond.

Roddenberry, having been a paramedic and former emergency room nurse who now serves as Lead Nurse at the FCS Tallahassee Cancer Center, and Campbell, a registered nurse at the FCS Orlando Orange clinic, made the perfect quick-response team.

The two carefully laid the passenger in the aisle and began their assessment, finding her vitals to be concerning — blood pressure and pulse rate were extremely low.

Thankfully, American Airlines was prepared. "I was both relieved and impressed with the amount of medical equipment available," Roddenberry said. The airplane's emergency kit contained an automated external defibrillator, IV supplies, IV fluids and epinephrine, among other medications and supplies.

Roddenberry and Campbell began the rapid administration of IV fluids, and the passenger-turned-patient started to improve — her blood pressure and blood flow began to stabilize. Roddenberry recalled, "She regained consciousness, became alert and oriented and her skin returned to that beautiful pink us nurses like to see!"

As the passenger began to recover, it became clear that she'd suffered from a vasovagal syncopal episode, where intense emotional triggers, like fear, can cause fainting and decreased heart rate and blood pressure.

With the patient stabilized, Roddenberry felt safe in advising the captain to continue their flight to their original destination, just under an hour away at this point. American Airlines colleagues on land in Dallas were informed and had emergency medical service personnel ready to assist.

Thanks to the quick reactions of the FCS nurses, the young woman was safely escorted off the plane for further evaluation. Their efforts didn't go unnoticed by their patient-in-flight, who found Roddenberry through Facebook not long after the incident, wanting to thank him.

"That warmed my heart to know she's okay," Roddenberry said. "We will continue to stay in touch!"

FCS has incorporated teamwork into its newly updated core values as it is an essential element in providing quality health care — this incident has proved that.

"I couldn't have succeeded without Angella's help," Roddenberry said. "She was beside me and assisted the entire time. She continued to monitor the patient and her vitals, communicating with me until we landed in Dallas. She was a rock star, indeed!"

While many see these nurses as heroes, the two remain humble in their actions.

Both received a letter from the medical director of American Airlines, which included a gift of 25,000 Skymiles in appreciation for their heroic efforts.

"Although not necessary, I am certainly very grateful," Roddenberry said. "We simply did what any other nurse would do in a time of need!"

"That's what we were trained to do, no matter what nursing specialty we later choose to practice," said Campbell, adding that, "as I always say, I'm always on duty; a nurse is always on duty."

SANFEL (PLANE) / ISTOCK / GETTY IMAGES PLUS

# FCS Foundation News & Events

**Our Mission:** *Providing nonmedical financial assistance for essential everyday living expenses to adults undergoing cancer treatment in Florida, to allow them to focus on fighting cancer. Due to the generosity of the Florida Cancer Specialists physicians, 100% of donations received go directly toward paying the essential nonmedical expenses of an adult battling cancer.*

FLORIDA CANCER SPECIALISTS Foundation


### Party Under the Stars 2023

February 25, 2023 | Hyatt Regency Sarasota


### Lyrics for Life

March 4, 2023 | Curtis M. Phillips Performing Arts Center, Gainesville

## Impact Spotlight

Miss Jessie, as she is known at the FCS Tallahassee Cancer Center, was still living in her home that was badly damaged from Hurricane Michael. She was standing in lines at her local food bank, having difficulty paying her bills and was about to have her electricity shut off. All this while battling multiple myeloma.

*"The first three years of chemo were incredibly tough and I'm not ashamed to tell you that I got behind on bills. I don't make a lot of money, and I never have. I was about to have my lights cut off when my financial counselor told me that the FCS Foundation could help me. The Foundation and all the people that donate are angels on earth and are helping so many people, not just me."*

— Jessie Thompson,
Grant Recipient

*"Miss Jessie has a spirit that lights up the room. She is always trying to make others feel good every time she walks into the clinic. It was a pleasure to help her, and you could tell she was relieved when her Foundation application was approved. Not having to worry about how to pay bills, like rent or utilities, absolutely helps patients in their healing."*

— Becky Lollie,
FCS Financial Navigator

**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, utilities and car payments. This financial assistance immediately impacts cancer patients and their families in communities throughout Florida, allowing them to focus on their recovery.

FCSF.org | Phone: 941-677-7181 /FLCancerFoundation /florida-cancer-specialists-foundation

# WELCOME NEW PHYSICIANS

**Alexander Philipovskiy, MD, PhD**
Hematologist and Medical Oncologist
*Lake Mary*

A Principal Investigator at the FCS Drug Development Unit in Lake Mary, Dr. Philipovskiy received his medical degree with honors before earning a doctorate in Medical Immunology and Microbiology from Odessa State Medical University in Odessa, Ukraine, where he also completed residency training in Internal Medicine. He completed a second Internal Medicine residency at New York Medical College and a fellowship in Medical Oncology and Hematology at New York Medical College Westchester Medical Center. Dr. Philipovskiy has served as a clinical observer at the National Cancer Institute in Bethesda, Maryland, at George Washington Medical Center in Washington, D.C., and at Drexel University College of Medicine in Philadelphia, Pennsylvania.

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**Richard McDonough, MD**
Hematologist and Medical Oncologist
*Zephyrhills Green Slope*

Dr. McDonough earned his medical degree from the University of Miami, where he also completed his residency training in Internal Medicine at Jackson Memorial Hospital. He completed a fellowship in Hematology and Oncology at the Mayo Clinic in Miami. Triple Board-certified, Dr. McDonough has been a leader in advocacy on behalf of cancer patients, ensuring convenient access to high-quality, affordable care. He served as president of the Florida Society of Clinical Oncology from 2017 to 2019 and as treasurer from 2014 to 2017. He currently serves as a committee member of the Community Oncology Alliance.

**Christopher McCann, DO**
Gynecologic Oncologist
*Lake Worth*

Dr. McCann holds a doctor of Osteopathic Medicine degree from the University of New England. He completed residency training in Obstetrics and Gynecology at Saint Francis Hospital in Hartford, Connecticut and a fellowship in Obstetrics and Gynecology at Massachusetts General Hospital in Boston. He has served as an Instructor in Obstetrics, Gynecology and Reproductive Biology at Harvard Medical School Hospital and on the medical staff of Beth Israel Deaconess Medical Center in Boston, Massachusetts. Dr. McCann specializes in the medical and surgical treatment of patients with ovarian, endometrial and cervical cancer, with a focus on the use of minimally invasive techniques.

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**Wenqing Zhang MD, PhD**
Hematologist and Medical Oncologist
*Crystal River, Lecanto*

After receiving his medical degree from Xinxiang Medical College in China, Dr. Zhang went on to earn both a master's and a doctorate in Medical Science from Beijing Medical University. He completed Internal Medicine residency training at Albert Einstein College of Medicine in The Bronx, New York, and a fellowship in Hematology and Oncology at the University of Louisville James Graham Brown Cancer Center in Louisville, Kentucky.

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**Monique Sajjad, DO**
Hematologist and Medical Oncologist
*Largo*

Dr. Sajjad joined FCS in 2018 as a hospitalist in Pinellas County. Dr. Sajjad received her medical degree from Lake Erie College of Osteopathic Medicine in Bradenton, Florida. She then completed her Internal Medicine residency training at the University of Southwest Florida in Tampa and a fellowship in Hematology and Oncology at the H. Lee Moffitt Cancer Center in Tampa.

**Mohammad Jahanzeb, MD, FACP**
Medical Oncologist
*Lake Worth Cancer Center, Delray Beach*

Dr. Jahanzeb received his medical degree from King Edward Medical College at Punjab University in Lahore, Punjab, Pakistan, and completed residency training at New Britain General Hospital at the University of Connecticut in New Britain. He was named as Senior Fellow during his fellowship in Hematology and Oncology at Washington University's Barnes Jewish Hospital in St. Louis, Missouri. Previously, Dr. Jahanzeb served as Chief of Medical Oncology Scientific and Strategic Advisor for GenesisCare. He was the Founder and former Managing Partner of Florida Precision Oncology Research and Consulting, LLC. He has held a number of academic appointments and currently serves as Clinical Affiliate Professor in the Department of Integrated Medicine at Charles E. Schmidt College of Medicine, Florida Atlantic University.

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**Ibrahim Sadek, MD**
Hematologist and Medical Oncologist
*Brownwood, Villages Cancer Center*

Board-certified in Medical Oncology, Hematology and Internal Medicine, Dr. Sadek received his medical degree from Suez Canal School of Medicine in Egypt before completing Internal Medicine residency training there and then another at the Georgia Regents University Hospital in Augusta, Georgia. He has completed fellowships at the Mayo Clinic College of Medicine for Hematology, at the University of Michigan for Geriatric Medicine and Palliative Care, and at Georgia Regents University Hospital for Hematology and Oncology. Prior to joining FCS, Dr. Sadek provided care to patients at Mayo Clinic Health System in Lacrosse, Wisconsin, and served as a consultant at Michiana Hematology Oncology Cancer Treatment Center in Mishawaka, Wisconsin.

**Susan K. Morgan, MD**
Hematologist and Medical Oncologist
*Bonita Springs, Naples*

After receiving her medical degree from Uniformed Services University of Health Sciences in Bethesda, Maryland, Dr. Morgan completed Internal Medicine residency training at Tripler Army Medical Center in Honolulu, Hawaii, and a fellowship in Hematology and Oncology at Walter Reed Army Medical Center in Washington, D.C. A former Lieutenant Colonel in the U.S. Army, she began her medical career as Chief of the Medical Specialty Clinic at Tripler Army Medical Center and later served as Assistant Chief of Hematology and Oncology Service at Walter Reed Army Medical Center. From 2002 to 2018 Dr. Morgan provided oncology care to patients at FCS in Naples and was actively involved in multiple clinical trials.

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**Shivtaj Mann, DO**
Hematologist and Medical Oncologist
*Fort Myers, Colonial, Cape Coral*

Dr. Mann received his Doctor of Osteopathic Medicine degree from NOVA Southeastern University in Fort Lauderdale, Florida. He completed residency training in Internal Medicine at Lehigh Valley Health Network in Allentown, Pennsylvania, and a fellowship in Hematology and Oncology at the University of Arizona in Tucson. Dr. Mann has a special interest in benign and malignant hematology as well as the diagnosis and treatment of lung and genitourinary cancers and melanoma. His research projects have been published in scientific journals, including the American Journal of Kidney Diseases.

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**Tony Kurian, MD**
Hematologist and Medical Oncologist
*Venice Island, Englewood*

Dr. Kurian received his medical degree from the University of South Florida Morsani College of Medicine in Tampa. While completing his Internal Medicine residency at Loyola University Medical Center in Mayville, Illinois, he was named as Chief Resident and served as a clinical preceptor for first- and second-year medical students. Dr. Kurian completed a fellowship in Hematology and Oncology with a specialty in blood and marrow transplantation and cellular immunotherapy at the University of South Florida Moffitt Cancer Center in Tampa, where he served as Chief Fellow.

# Cancer Care Expanded

FCS keeps growing with new locations in Kissimmee and Zephyrhills

## KISSIMMEE

Florida Cancer Specialists & Research Institute (FCS) celebrated the opening of its new location in Kissimmee with a ribbon cutting ceremony in June. The 3,400-square-foot office, located at 801 W. Oak St., offers a wide range of treatments, including medical oncology and hematology, infusions and in-house laboratory services.

"This new location further expands our presence in the heart of central Florida," said FCS Chief Executive Officer Nathan H. Walcker. "Patients in Osceola County can now benefit from easy access to world-class cancer care close to home."

"We are extremely excited about this latest expansion to our statewide community oncology network," said FCS President and Managing Physician Michael Diaz, MD. "Our cancer care experts provide the most advanced treatments and therapies personalized for each patient's unique needs."

Care is being provided to patients at the new Kissimmee location by FCS Board-certified Medical Oncologists Geetha Akula, MD; Martin Dietrich, MD, PhD; Aamer Farooq, MD; and Michel Velez, MD.

Among the community members and health care colleagues who attended the event was Kissimmee/Osceola County Chamber of Commerce Senior Director of Business Development Robin Hughes, who stated that "having such high-quality cancer care in our immediate backyard will be highly beneficial for Osceola County."

Kissimmee

Zephyrhills Green Slope

## ZEPHYRHILLS GREEN SLOPE

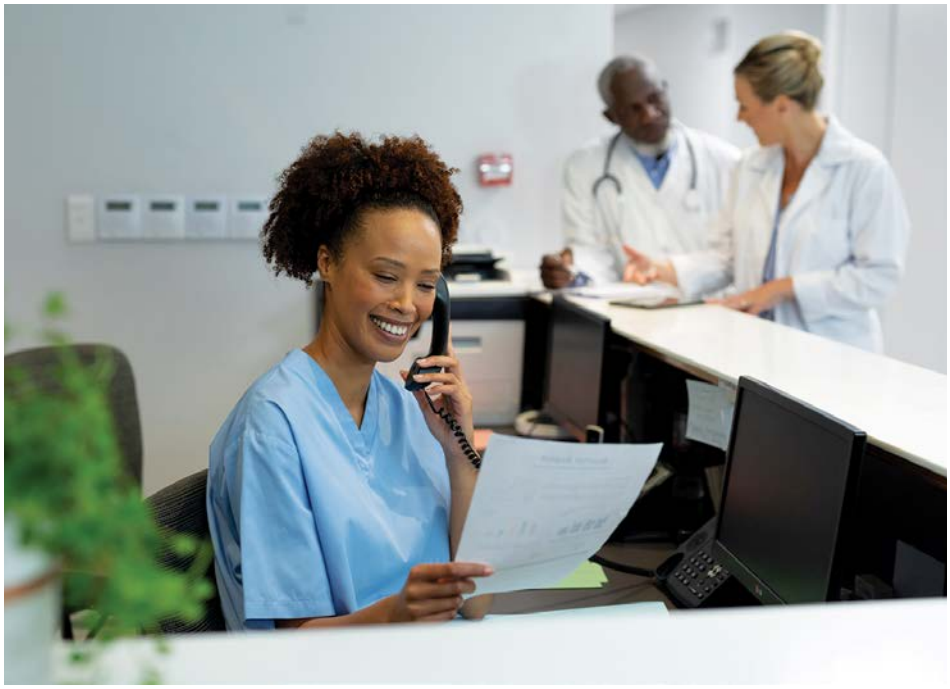
Florida Cancer Specialists & Research Institute (FCS) held a ribbon cutting ceremony in August to celebrate the opening of their new Pasco County clinic located at 7315 Green Slope Drive in Zephyrhills.

FCS Board-certified Medical Oncologist Richard McDonough, MD, is providing care to patients with cancer and blood disorders at the new Zephyrhills Green Slope clinic, offering a range of treatments and services including medical oncology and hematology, infusions, in-house laboratory, oral oncolytic specialty pharmacy, care management and access to clinical trials.

Nearing 100 locations across the state of Florida, FCS is excited to be expanding on accessibility for cancer patients statewide.

"Our practice will now provide world-class cancer care to even more local residents in a truly impressive, patient-centric environment," said FCS Chief Executive Officer Nathan H. Walcker. "This new location is a testament to FCS' commitment to patients in the Zephyrhills community and throughout Pasco County."

"Our new clinic location provides a warm and welcoming environment. Every detail is focused on the patient's experience so that each can achieve the very best outcome," said Michael Diaz, MD, FCS President and Managing Physician.



# Grads to Work Program

Florida Cancer Specialists & Research Institute (FCS) is teaming up with Strayer University on their Grads to Work program to help prepare students for job opportunities and support them in continuing education.

"Grads to Work will enable us to expand and diversify our talent pool to fill critical job openings while providing a results-oriented pathway for students to receive the foundation they need to thrive and grow in their future careers," said FCS Senior Vice President of Organizational Effectiveness and Learning, Marilyn Morales, MS, MBA, LBBP, CPT.

The program will be catered to those interested in long-term employment in health care and who may not otherwise have the means to support an education. Grads to Work will provide candidates with a pathway to a non-clinical associate degree while they work for FCS as patient service representatives.

Candidates will complete a five-week workforce readiness course and will be eligible to interview for open positions with FCS at their locations in the Greater Tampa Bay area. As the program expands, more positions will become available at FCS' nearly 100 locations across Florida.

Upon hire, program participants can pursue an associate degree with Strayer University, at no cost to them. These students will be able to gain working experience and receive mentorship while pursuing their fully funded degree.

"Partnerships like the one we have formed with Strayer University are critical and reflect our efforts to combat the diminishing health care workforce, to build it back up again, possibly even seeing some of these students return to FCS to begin their careers following graduation," said Morales.

PHOTOS BY WAVEBREAKMEDIA (GRADS) AND GEORGE DOYLE (RX) / ISTOCK / GETTY IMAGES PLUS

# FCS Receives URAC Accreditation for RX To Go

Florida Cancer Specialists & Research Institute (FCS) has earned the Utilization Review Accreditation Commission's (URAC) accreditation for specialty pharmacy for the FCS oral oncolytic specialty pharmacy, RX To Go.

The URAC is an independent leader in promoting health care quality by setting high standards for clinical practice, consumer protections, performance measurement, operations infrastructure and risk management.

Oral anti-cancer medications are essential to cancer care, as they currently comprise 25% to 35% of oncology treatments. With FCS' centralized state-of-the-art pharmacy, based in Fort Myers, Florida, patients have ready access to 99% of the available oral oncolytics, which can be quickly dispensed and sent directly to their homes. Rx To Go works exclusively on behalf of FCS' 250 physicians and their patients to ensure quality, safety and effective treatment outcomes.

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

# From Our Patients

Jorge Ayub, MD

Dear Dr. Ayub,

My family received a letter from Florida Cancer Specialists Foundation letting us know you have so generously donated to the foundation in honor of our mother's memory.

What a beautiful and meaningful gesture. Mother thought of you with fondness, admiring your gentle and kind manor. She took comfort in knowing you were always thinking of her well-being, physically and spiritually. She always had a smile on her face upon leaving your office as you and your fabulous staff were always so uplifting!

Thank you for the healing you gave Mother on her journey!

Thank you, for your donation in her memory, giving hope and blessings to those who are battling cancer!

Most fondly,
Annie Pollard and family
Daughter of Evelyn K. Startzman

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★★★★★

GOOGLE REVIEW: 5 STARS

I'm telling you, God is in the sky over us. Not only is Dr. Dodd such a comforting doctor and gets right to the point of what will help you, but on top of that, his entire staff there is just amazing. I can't say that enough. I know a lot of people have lost their drive to even do medical as a profession since COVID, but having an extreme anxiety disorder, I can't thank this staff enough for your empathy for people and listening to you all talk to other patients and comforting them. Thank you, and may God bless your efforts and kindness.

Paul M. Dodd, MD

★★★★★

GOOGLE REVIEW: 5 STARS

Dr. Gupta is compassionate and professional. She goes above and beyond for her patients. I highly recommend her.

Eva Gupta, MD

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★★★★★

GOOGLE REVIEW: 5 STARS

The first time at the office, the front staff was excellent. The lab tech was excellent. Dr. Chamberlain was wonderful — made you feel at ease, explained everything thoroughly, did not hurry you or make you feel rushed. I was so pleased with this office.

Kerry E. Chamberlain, DO

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★★★★★

DOCTOR WEBMD REVIEW: 5 STARS

I have seen Dr. Gupta several times now in the course of my treatment. She is comprehensive in her review of my situation and practical in her recommendations. She is direct, but warm and approachable. Very different from the experience I had with another oncologist years ago.

Shaachi Gupta, MD, MPH

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★★★★★

GOOGLE REVIEW: 5 STARS

I was most impressed that Dr. Stine took time to carefully explain all my options. Not only is she a superior surgeon, but she is a caring person. I appreciate, so much, both her care and her skill.

Jessica Stine, MD

★★★★★

GOOGLE REVIEW: 5 STARS

Lalit Aneja, MD

My brother received a diagnosis of stage 4 colon cancer through the Department of Veterans Affairs. The VA referred him to Dr. Aneja with Florida Cancer Specialists & Research Institute. We showed up for the first appointment armed with everything our friends, family and Google had recommended based on research. Well, we were wrong. Dr. Aneja gently educated us on the proven ways to attack the specific cancer which my brother had, and we yielded to his advice. We are now three months in, or halfway through his treatments. The cancer is 97% gone and the markers are about the range of a normal person. We are so grateful for Dr. Aneja's expertise in his field, his gentleness, compassion and, above all else, the results we have received.

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★★★★★

HEALTHGRADES REVIEW: 5 STARS

Joseph M. Sennabaum, MD

He is straight forward, honest and caring. If you don't want to hear the truth or be coddled, go somewhere else. My experience with other major institutions was all based on lies and false hope. Dr. Sennabaum will not lie to you and he is the smartest human being I have ever met. His staff is amazing, every person in that office makes you feel cared about and respected. You will not get a better oncologist.

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★★★★★

HEALTHGRADES REVIEW: 5 STARS

Vivian Griffin, MD

Dr. Griffin is the most caring and informative doctor I have ever been to. She is thorough and explains things, and you actually understand your conditions. Even her staff takes great care of you. She is a wonderful doctor and will be the only one I go to for any treatments I need. Thank you, Dr. Griffin for your compassion during my hard time.

★★★★★

FACEBOOK REVIEW: 5 STARS

Janice F. Eakle, MD

To me, FCS is the best place to get the care you need. Dr. Eakle has been on top of my hemolytic anemia since 2010. I was in remission until my RA doctor gave me methotrexate, which caused my blood count to drop down to a little below eight. We've tried everything to get it back up. Dr. Eakle, in conjunction with another doctor at Moffitt, has made a plan that now has me back on top and I am holding steady in the 11 range. I couldn't ask for a better doctor, she is fantastic. Thank you.

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★★★★★

HEALTHGRADES REVIEW: 5 STARS

Yaman Suleiman, MD

Dr. Suleiman has been my mother's oncologist since 2017. She was diagnosed with Stage 4 lung cancer. Dr. Suleiman's name represents a "man of peace." This is truly what he has given my mother and family — a "peace of mind." He was there physically, mentally and intellectually for us. He treated my mother with the best of his ability, knowledge and experience. He kept me abreast with all her treatments whether I was at her visit or not. I could always call his support staff for any concerns which I may have, and they would respond to me in a very, very reasonable time. Trust and believe me; today, my mother's scans are showing no cancer. I know God put Dr. Suleiman here to give his people the comfort, trust, treatment and peace he has stored upon him. Thank you, Dr. Suleiman, for everything! We are so grateful and thankful for your service.

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★★★★★

GOOGLE REVIEW: 5 STARS

Miguel Pelayo, MD

Dr. Pelayo is the best caring and knowledgeable doctor I have ever been to. He tells you your options and his recommendations, then respects your decisions and individual treatment based on you as an individual.

# Online Reviews Enhance FCS' Reputation and Growth

How does a newly diagnosed cancer patient choose an oncologist?

Word-of-mouth recommendations remain one of the most powerful and effective marketing tools in health care. And in this digital age, prospective patients turn to online reviews to assess the capabilities and qualifications of health care providers and practices.

Maintaining a strong and healthy online reputation for Florida Cancer Specialists is a strategic focus of the FCS Marketing team. Proactive online-reputation management is one of several key initiatives helping to ensure that prospective patients can easily discover FCS in their local area and learn why we are their best choice for oncology care.

"Patient reviews are a significant factor influencing how FCS ranks in search results and we proactively encourage patients to post online reviews about us," said FCS Director of Marketing Kat Romanowski-Wade. "Their perspectives are authentic and fresh, and they showcase what is unique and special about our FCS physicians and clinics."

Efforts don't stop there, however. "We are constantly listening and responding to feedback," said Romanowski-Wade.

Each review — positive or not — is responded to promptly.

"By actively listening and engaging with patients, we are strengthening our relationships and gaining valuable insights into what we are doing well and what we can be doing to improve."

The overall online health of FCS continues to improve and grow on platforms including Google, Healthgrades, WebMD, Sharecare and others. Here are some recent statistics from quarter three, 2022:

- Received over **9,000** profile views to our combined FCS locations' pages online with 314 profile actions at a **3.4%** conversion rate *(industry average is 3.1%)*.
- Over **142,000** views to our FCS provider profiles, at a **4.1%** conversion rate *(industry average is 3.1%)*.
- Google has been the top performing site for us with over **338,000** total profile views and over **18,000** profile actions at a **5.5%** conversion rate *(industry average is 3%)*.

***Reports Created by Press Ganey Consumer Solutions***

***DEFINITION:***

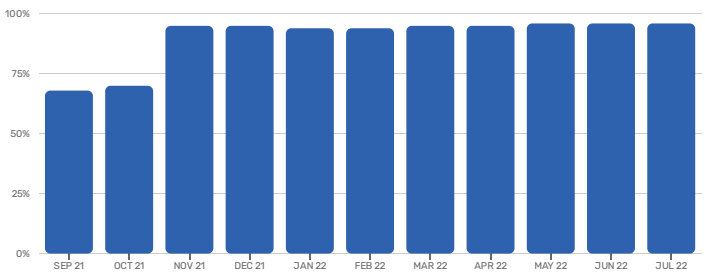
***Listing Accuracy***
*This is the proportion of accurate core profile data points for a provider or location across the leading listing sites. Sites with more traffic and a greater presence in the market account for a larger proportion of the Listing Accuracy score. The core data points are generally the name, address and phone number.*

*A Listing Accuracy of over 80% is very good. Because of how sites consume data sources, it is very often not possible for a provider or location to achieve 100% accuracy.*

## PROVIDER LISTING ACCURACY

93
Total Locations

96%
Average Listing Accuracy




### PROVIDER LISTING STATUS

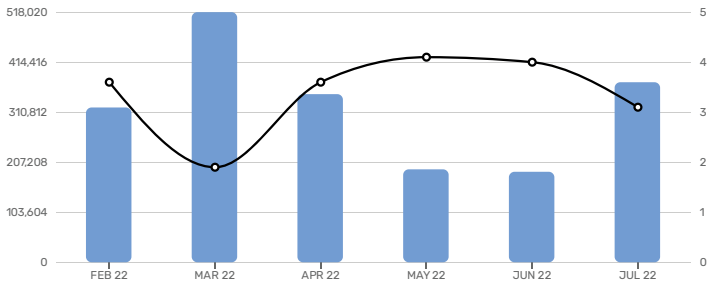
| Site | Average Accuracy | Profiles Reporting | Profiles in Progress |
|---|---|---|---|
| Google | 94% | 237 | 0 |
| Healthgrades | 82% | 237 | 0 |
| WebMD | 83% | 231 | 6 |
| Vitals | 85% | 236 | 1 |
| Ratemds | 57% | 120 | 26 |
| CareDash | 87% | 232 | 5 |
| Sharecare | 79% | 140 | 6 |
| Wellness | 96% | 142 | 4 |

## PROVIDER LISTING PERFORMANCE

237
Total Providers

1.8M Total Profile Views

1.7% Average Conversion Rate




### LISTING SITE PERFORMANCE

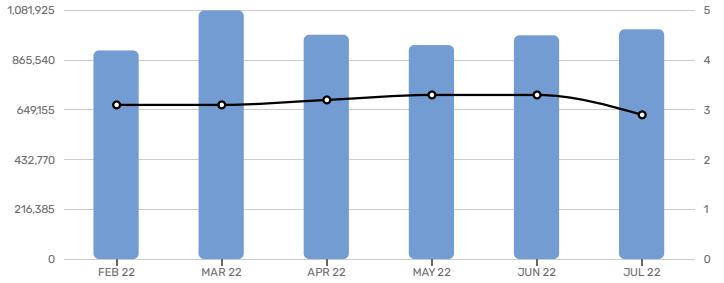
| Site | Profile Views | Profile Actions | Conversion | Average Views Per Profile | Average Actions Per Profile |
|---|---|---|---|---|---|
| Google | 4,337,868 | 217,398 | 5.0% | 18,303 | 917 |
| *945,549 Search Views* | *234,685 Map Views* | *32,362 Website Link Clicks* | *37,253 Phone Number Clicks* | | |
| Healthgrades | 445,448 | 21,260 | 4.8% | 1,880 | 90 |
| WebMD | 51,752 | 116 | 0.2% | 219 | 0 |
| Vitals | 21,928 | 282 | 1.3% | 93 | 1 |
| Ratemds | 2,914 | 122 | 4.2% | 14 | 1 |
| CareDash | 34,256 | 1,402 | 4.1% | 145 | 6 |
| Sharecare | 102,806 | 4,882 | 4.7% | 434 | 21 |
| Wellness | 2,040 | 58 | 2.8% | 10 | 0 |
| YP | 15,654 | 442 | 2.8% | 67 | 2 |

## LOCATION LISTING PERFORMANCE

92
Total Locations

5.8M Total Profile Views

2.7% Average Conversion Rate




### LISTING SITE PERFORMANCE

| Site | Profile Views | Profile Actions | Conversion | Average Views Per Profile | Average Actions Per Profile |
|---|---|---|---|---|---|
| Google | 5,860,892 | 191,365 | 3.3% | 63,705 | 2,080 |
| *1,737,817 Search Views* | *3,539,800 Map Views* | *61,411 Website Link Clicks* | *67,051 Phone Number Clicks* | | |

***DEFINITIONS:***

***Profile Views***
*This is the number of times the listing site profiles have been viewed. Because of different methods of reporting by our partners, these views may not be unique – that is, a single patient could generate multiple views.*

*Generally, profiles with better review ratings, a profile photo and detailed contact information will generate more traffic. Specialty, geographic location and other factors can also have a large effect on profile views.*

*Two providers with similar profiles working in the same area might have very different profile traffic if, for example, their specialties are different.*

***Profile Actions***
*This is the number of times that we and our partners measured an action on a listing site profile. This can include clicks on the website link, the phone number, or an appointment request button. The type of data reported depends on partner site, and some sites do not provide detailed analytics. For those, we generate intelligent estimates based on known site traffic and other statistics.*

***Conversion Rate***
*This is the number of profile actions divided by the number of profile views — that is, how many views generated an action by a prospective patient.*

*While the health care industry average for conversion is around 3%, this can depend a lot on specialty and services offered.*

# Thank You to our 2022 FCS Operations Team Meeting Sponsors

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FLORIDA CANCER SPECIALISTS & Research Institute

2022 OPERATIONS MEETING

INVITAE

# The answers you need, the support you expect

## Comprehensive cancer genetic testing

1 in 8 patients with cancer has a genetic mutation passed down through their family.[1] Invitae germline panels provide **tools for you to give your patients answers reliably and quickly**

- Out-of-pocket cost estimator tool for breast, ovarian and colorectal cancer
- All commercial insurance, Medicaid and Medicare plans accepted
- Optional comprehensive post-test genetic counseling session for patients at no additional charge
- Easy-to-use online ordering and results delivery

## Personalized Cancer Monitoring (PCM™): Get ahead of cancer

**Invitae PCM** is a pan-cancer,* tumor-informed liquid biopsy test that detects circulating tumor DNA (ctDNA) to assess for minimal or molecular residual disease (MRD) in patients with cancer.

- Personalized: customized to each tumor signature
- Highly sensitive and specific: detects ctDNA at 0.008% concentration in plasma with >99.9% analytical specificity[2]

**Browse our catalog at invitae.com/tests**

**Contact your local Invitae rep.**
Call client services at 1-800-436-3037
or visit invitae.com/en/contact.

**Exceptions exist, like CNS malignancies and sarcomas. This test is not intended to be used in hematological malignancies such as leukemias or lymphomas.*


1. Samadder NJ, *et al.* Comparison of Universal Genetic Testing vs Guideline-Directed Targeted Testing for Patients With Hereditary Cancer Syndrome [published correction appears in *JAMA Oncol.* 2021 Feb 1;7(2):312]. *JAMA Oncol.* 2021;7(2):230-237.
2. Data on file.


AD155-1 August 2022


# This is why we do what we do.

Each day we get up with the same goal in mind.

Our focus is on helping patients who have to deal with some of the toughest challenges of their lives. The patient has a constant, daily battle to fight, even when the hardships make it seem impossible. It is the support of their family, friends, and community that gives them a chance to thrive in the future.

At FCS, it takes a full team of doctors, nurses, front-line workers – and an extended community of clinic staff, corporate teams, IT, and leadership – all with the experience and knowledge to support patients on their journey to recovery.

We wake up daily with a passion and vigor to sustain that mission, and drive a deeper impact from all of FCS' efforts. Our partnership affects the patient experience, and our synergies and shared principles are what make this partnership great. For that, we extend a heartfelt thank you.

**Ascend Technologies Group** is proud to partner with **Florida Cancer Specialists** and its patients. We look forward to thriving with you in 2023 and beyond.

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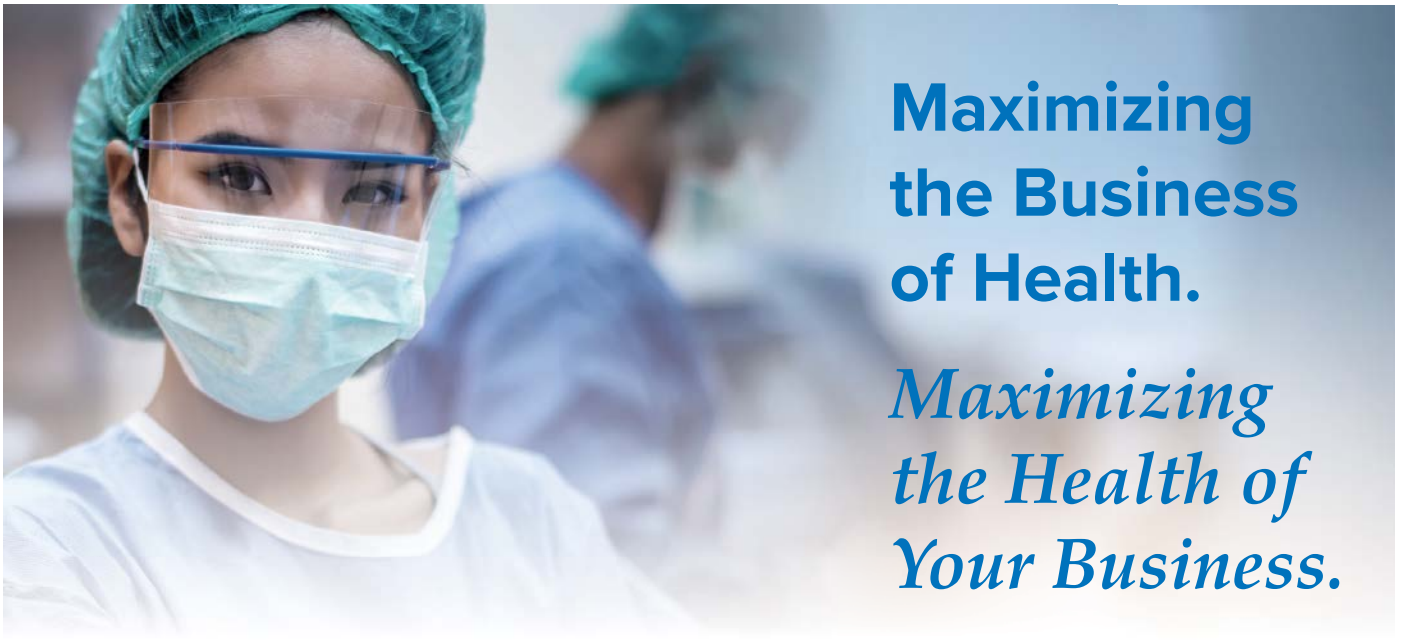

# Maximizing the Business of Health.

## *Maximizing the Health of Your Business.*

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HENRY SCHEIN® MEDICAL

GF-HSM1021

tivdak®
tisotumab vedotin-tftv
for injection 40 mg

# A Spark of Change

**Tivdak—the first-and-only antibody-drug conjugate** for adults with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.*

## RESPONSE RATE AND OTHER OUTCOMES FROM THE innovaTV 204 TRIAL[1-3,a]

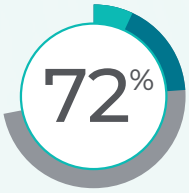
**Tivdak was studied in a global, open-label, multicenter, single-arm clinical trial (N=101)**

### Primary Endpoint by IRC


- 7% Complete Response (CR) (n=7/101)
- 17% Partial Response (PR) (n=17/101)

Disease control rate (DCR), which includes stable disease (SD), is an exploratory post-hoc calculation and not a pre-specified endpoint. In the setting of a single-arm trial without a comparable control arm, as in a randomized trial, interpretation and clinical relevance of some endpoints is unclear. It is unknown if SD is a result of natural disease progression or treatment with Tivdak.


**SD**
(n=49/101)




**DCR**
(n=73/101) (95% CI: 63-81)
DCR=24% ORR + 49% SD

DCR was defined as the total ORR, which was the sum of CR and PR, plus SD. Per RECIST v1.1, SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD). SD was measured at least 5 weeks after the first dose of treatment.

[a]The efficacy of Tivdak was evaluated in 101 patients with recurrent or metastatic cervical cancer who received no more than two prior systemic regimens in the recurrent or metastatic setting, including at least one prior platinum-based chemotherapy regimen. Patients were excluded if they had active ocular surface disease, any prior episode of cicatricial conjunctivitis, or Stevens Johnson syndrome, Grade 2 or higher peripheral neuropathy, or known coagulation defects leading to an increased risk of bleeding.

[b]ORR consisted of confirmed CR or PR per RECIST v1.1. CR was defined as the disappearance of all target and nontarget lesions. PR was defined as a ≥30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters.

## *Indication

TIVDAK is indicated for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

**tivdakHCP.com**

## Important Safety Information

### BOXED WARNING: OCULAR TOXICITY

**TIVDAK caused changes in the corneal epithelium and conjunctiva resulting in changes in vision, including severe vision loss, and corneal ulceration. Conduct an ophthalmic exam at baseline, prior to each dose, and as clinically indicated. Adhere to premedication and required eye care before, during, and after infusion. Withhold TIVDAK until improvement and resume, reduce the dose, or permanently discontinue, based on severity.**

**See additional Important Safety Information on next page, and Brief Summary for TIVDAK on adjacent pages.**

# Important Safety Information, cont.

## Warnings and Precautions

**Ocular Adverse Reactions** occurred in 60% of patients with cervical cancer treated with TIVDAK across clinical trials. The most common were conjunctival adverse reactions (40%), dry eye (29%), corneal adverse reactions (21%), and blepharitis (8%). Grade 3 ocular adverse reactions occurred in 3.8% of patients, including severe ulcerative keratitis in 3.2% of patients. One patient experienced ulcerative keratitis with perforation requiring corneal transplantation. Cases of symblepharon were reported in patients with other tumor types treated with TIVDAK at the recommended dose.

In innovaTV 204, 4% of patients experienced visual acuity changes to 20/50 or worse including 1% of patients who experienced a visual acuity change to 20/200. Of the patients who experienced decreased visual acuity to 20/50 or worse, 75% resolved, including the patient who experienced decreased visual acuity to 20/200.

Refer patients to an eye care provider for an ophthalmic exam including visual acuity and slit lamp exam at baseline, prior to each dose, and as clinically indicated. Adhere to premedication and required eye care to reduce the risk of ocular adverse reactions. Promptly refer patients to an eye care provider for any new or worsening ocular signs and symptoms. Withhold dose, reduce the dose, or permanently discontinue TIVDAK based on the severity of the adverse reaction.

**Peripheral Neuropathy (PN)** occurred in 42% of cervical cancer patients treated with TIVDAK across clinical trials; 8% of patients experienced Grade 3 PN. PN adverse reactions included peripheral neuropathy (20%), peripheral sensory neuropathy (11%), peripheral sensorimotor neuropathy (5%), motor neuropathy (3%), muscular weakness (3%), and demyelinating peripheral polyneuropathy (1%). One patient with another tumor type treated with TIVDAK at the recommended dose developed Guillain-Barre syndrome. Monitor patients for signs and symptoms of neuropathy. For new or worsening PN, withhold, dose reduce, or permanently discontinue TIVDAK based on the severity of PN.

**Hemorrhage** occurred in 62% of cervical cancer patients treated with TIVDAK across clinical trials. The most common all grade hemorrhage adverse reactions were epistaxis (44%), hematuria (10%), and vaginal hemorrhage (10%). Grade 3 hemorrhage occurred in 5% of patients.

Monitor patients for signs and symptoms of hemorrhage. For patients experiencing pulmonary or CNS hemorrhage, permanently discontinue TIVDAK. For Grade ≥2 hemorrhage in any other location, withhold until bleeding has resolved, blood hemoglobin is stable, there is no bleeding diathesis that could increase the risk of continuing therapy, and there is no anatomical or pathologic condition that can increase the risk of hemorrhage recurrence. After resolution, either resume treatment or permanently discontinue TIVDAK.

**Pneumonitis:** Severe, life-threatening, or fatal pneumonitis can occur in patients treated with antibody-drug conjugates containing vedotin, including TIVDAK. Among patients with cervical cancer treated with TIVDAK across clinical trials, 2 patients (1.3%) experienced pneumonitis, including 1 patient who had a fatal outcome.

Monitor patients for pulmonary symptoms of pneumonitis. Infectious, neoplastic, and other causes for symptoms should be excluded through appropriate investigations.

Withhold TIVDAK for patients who develop persistent or recurrent Grade 2 pneumonitis and consider dose reduction. Permanently discontinue TIVDAK in all patients with Grade 3 or 4 pneumonitis.

**Embryo-Fetal Toxicity:** TIVDAK can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TIVDAK and for 2 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TIVDAK and for 4 months after the last dose.

## Adverse Reactions

Serious adverse reactions occurred in 43% of patients; the most common (≥3%) were ileus (6%), hemorrhage (5%), pneumonia (4%), PN, sepsis, constipation, and pyrexia (each 3%). Fatal adverse reactions occurred in 4% of patients who received TIVDAK, including septic shock, pneumonitis, sudden death, and multisystem organ failure (each 1%).

Adverse reactions leading to permanent discontinuation occurred in 13% of patients receiving TIVDAK; the most common (≥3%) were PN (5%) and corneal adverse reactions (4%). Adverse reactions leading to dose interruption occurred in 47% of patients; the most common (≥3%) were PN (8%), conjunctival adverse reactions (4%), and hemorrhage (4%). Adverse reactions leading to dose reduction occurred in 23% of patients; the most common (≥3%) were conjunctival adverse reactions (9%) and corneal adverse reactions (8%).

The most common (≥25%) adverse reactions, including laboratory abnormalities, were hemoglobin decreased (52%), fatigue (50%), lymphocytes decreased (42%), nausea (41%), PN (39%), alopecia (39%), epistaxis (39%), conjunctival adverse reactions (37%), hemorrhage (32%), leukocytes decreased (30%), creatinine increased (29%), dry eye (29%), prothrombin international normalized ratio increased (26%), activated partial thromboplastin time prolonged (26%), diarrhea (25%), and rash (25%).

## Drug interactions

**Strong CYP3A4 Inhibitors:** Concomitant use with strong CYP3A4 inhibitors may increase unconjugated monomethyl auristatin E (MMAE) exposure, which may increase the risk of TIVDAK adverse reactions. Closely monitor patients for TIVDAK adverse reactions.

## Use in Specific Populations

**Moderate or Severe Hepatic Impairment:** MMAE exposure and adverse reactions are increased. Avoid use.

**Lactation:** Advise lactating women not to breastfeed during TIVDAK treatment and for at least 3 weeks after the last dose.

**Please see Brief Summary, including BOXED WARNING for TIVDAK on the following pages.**

CI, confidence interval; IRC, independent review committee; ORR, objective response rate.

**References: 1.** TIVDAK [Prescribing Information]. Bothell, WA: Seagen Inc. January 2022. **2.** Coleman RL, Lorusso D, Gennigens C, et al. Efficacy and safety of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer (innovaTV 204/GOG-3023/ENGOT-cx6): a multicentre, open-label, single-arm, phase 2 study. *Lancet Oncol.* 2021;22(5):609-619. **3.** Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer.* 2009;45(2):228-247.



Seagen | Genmab

tivdak®
tisotumab vedotin-tftv
for injection 40 mg

**TIVDAK® (tisotumab vedotin-tftv) for injection, for intravenous use**

The following is a Brief Summary of the full Prescribing Information. **Please See full Prescribing Information including BOXED WARNING. Rx Only.**

**WARNING: OCULAR TOXICITY**

- **TIVDAK caused changes in the corneal epithelium and conjunctiva resulting in changes in vision, including severe vision loss, and corneal ulceration.**
- **Conduct an ophthalmic exam at baseline, prior to each dose, and as clinically indicated.**
- **Adhere to premedication and required eye care before, during, and after infusion.**
- **Withhold TIVDAK until improvement and resume, reduce the dose, or permanently discontinue, based on severity.**

## INDICATIONS AND USAGE

TIVDAK is a tissue factor-directed antibody and microtubule inhibitor conjugate indicated for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

## DOSAGE AND ADMINISTRATION

### Recommended Dosage

The recommended dose of TIVDAK is 2 mg/kg (up to a maximum of 200 mg for patients ≥100 kg) administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity.

### Premedication and Required Eye Care

Adhere to the following recommendations to reduce the risk of ocular adverse reactions.

- Ophthalmic Exam: Conduct an ophthalmic exam including visual acuity and slit lamp exam at baseline, prior to each dose, and as clinically indicated.
- Topical corticosteroid eye drops: The initial prescription and all renewals of any corticosteroid medication should be made only after examination with a slit lamp. Administer first drop in each eye prior to each infusion. Instruct patients to continue to administer eye drops in each eye as prescribed for 72 hours after each infusion.
- Topical ocular vasoconstrictor drops: Administer in each eye immediately prior to each infusion.
- Cold packs: Use cooling eye pads during the infusion of TIVDAK.
- Topical lubricating eye drops: Instruct patients to administer for the duration of therapy and for 30 days after the last dose of TIVDAK.
- Contact Lenses: Advise patients to avoid wearing contact lenses unless advised by their eye care provider for the entire duration of therapy.

### Dosage Modifications for Adverse Reactions

The recommended TIVDAK dose reduction schedule is provided in Table 1.

**Table 1: Dosage Reduction Schedule**

| | **TIVDAK Dose Level** |
|---|---|
| Starting dose | 2 mg/kg |
| First dose reduction | 1.3 mg/kg |
| Second dose reduction | 0.9 mg/kg* |

* Permanently discontinue in patients who cannot tolerate 0.9 mg/kg

The recommended dose modifications for adverse reactions are provided in Table 2.

**Table 2: Dosage Modifications for Adverse Reactions**

| **Adverse Reaction** | **Severity** | **Occurrence** | **TIVDAK Dose Modification** |
|---|---|---|---|
| **Keratitis*** | Superficial punctate keratitis (SPK) | Any | Monitor. |
| | Confluent superficial keratitis | First occurrence | Withhold dose until SPK or normal, then resume treatment at the next lower dose level. |
| | | Second occurrence | Permanently discontinue |
| | Ulcerative keratitis or perforation | Any | Permanently discontinue. |
| **Conjunctival ulceration*** | Any ulceration | First occurrence | Withhold dose until complete conjunctival re-epithelialization, then resume treatment at the next lower dose level. |
| | | Second occurrence | Permanently discontinue. |
| **Conjunctival or corneal scarring or symblepharon*** | Any scarring or symblepharon | Any | Permanently discontinue. |
| **Conjunctivitis and other ocular adverse reactions*** | Grade 1 | Any | Monitor. |
| | Grade 2 | First occurrence | Withhold dose until Grade ≤1, then resume treatment at the same dose. |
| | | Second occurrence | Withhold dose until Grade ≤1, then resume treatment at the next lower dose level. If no resolution to Grade ≤1, permanently discontinue. |
| | | Third occurrence | Permanently discontinue. |
| | Grade 3 or 4 | Any | Permanently discontinue. |

**Table 2 continued on next page**

**continuation of Table 2 from previous page**

| | | | |
|---|---|---|---|
| **Peripheral Neuropathy** | Grade 2 | Any (initial or worsening of pre-existing condition) | Withhold dose until Grade ≤1, then resume treatment at the next lower dose level. |
| | Grade 3 or 4 | Any | Permanently discontinue. |
| **Hemorrhage** | Any grade pulmonary or CNS | Any | Permanently discontinue. |
| | Grade 2 in any other location | Any | Withhold until resolved, then resume treatment at the same dose. |
| | Grade 3 in any other location | First occurrence | Withhold dose until resolved, then resume treatment at the same dose. |
| | | Second occurrence | Permanently discontinue. |
| | Grade 4 in any other location | Any | Permanently discontinue. |
| **Pneumonitis** | Grade 2 | Any | Withhold dose until Grade ≤1 for persistent or recurrent pneumonitis, consider resuming treatment at next lower dose level. |
| | Grade 3 or 4 | Any | Permanently discontinue |

*Refer patients to an eye care provider promptly for an assessment of new or worsening ocular symptoms.

## WARNINGS AND PRECAUTIONS

### Ocular Adverse Reactions

Ocular adverse reactions occurred in 60% of patients with cervical cancer treated with TIVDAK across clinical trials. The most common ocular adverse reactions were conjunctival adverse reactions (40%), dry eye (29%), corneal adverse reactions (21%), and blepharitis (8%). Grade 3 ocular adverse reactions occurred in 3.8% of patients, including severe ulcerative keratitis in 3.2% of patients. One patient experienced ulcerative keratitis with perforation requiring corneal transplantation. Cases of symblepharon were reported in patients with other tumor types treated with TIVDAK at the recommended dose.

The median time to onset of the first ocular adverse reaction was 1.2 months (range, 0 – 6.5). Of the patients who experienced ocular events, 55% had complete resolution and 30% had partial improvement (defined as a decrease in severity by one or more grades from the worst grade) at last follow up. Ocular adverse reactions led to discontinuation of TIVDAK in 6% of patients with cervical cancer.

In innovaTV 204, 4% of patients experienced visual acuity changes to 20/50 or worse including 1% of patients who experienced a visual acuity change to 20/200. Of the patients who experienced decreased visual acuity to 20/50 or worse, 75% resolved, including the patient who experienced decreased visual acuity to 20/200.

Refer patients to an eye care provider for an ophthalmic exam including visual acuity and slit lamp exam at baseline, prior to each dose, and as clinically indicated. Adhere to premedication and required eye care to reduce the risk of ocular adverse reactions.

Promptly refer patients to an eye care provider for any new or worsening ocular signs and symptoms.

Withhold, reduce the dose, or permanently discontinue TIVDAK based on the severity of the adverse reaction.

### Peripheral Neuropathy

Peripheral neuropathy occurred in 42% of patients with cervical cancer treated with TIVDAK across clinical trials; 8% of patients experienced Grade 3 peripheral neuropathy. Peripheral neuropathy adverse reactions included peripheral neuropathy (20%), peripheral sensory neuropathy (11%), peripheral sensorimotor neuropathy (5%), motor neuropathy (3%), muscular weakness (3%), and demyelinating peripheral polyneuropathy (1%). One patient with another tumor type treated with TIVDAK at the recommended dose developed Guillain-Barre syndrome.

The median time to onset of peripheral neuropathy was 2.4 months (range, 0-11.3). Of the patients who experienced peripheral neuropathy, 17% had complete resolution and 17% had partial improvement (defined as a decrease in severity by one or more grades from the worst grade) at last follow up. Peripheral neuropathy led to discontinuation of TIVDAK in 8% of patients with cervical cancer.

Monitor patients for signs and symptoms of neuropathy, such as paresthesia, tingling or a burning sensation, neuropathic pain, muscle weakness, or dysesthesia. For patients experiencing new or worsening peripheral neuropathy, withhold dose, then dose reduce, or permanently discontinue TIVDAK based on the severity of peripheral neuropathy.

### Hemorrhage

Hemorrhage occurred in 62% of patients with cervical cancer treated with TIVDAK across clinical trials. The most common all grade hemorrhage adverse reactions were epistaxis (44%), hematuria (10%), and vaginal hemorrhage (10%). Grade 3 hemorrhage occurred in 5% of patients.

The median time to onset of hemorrhage was 0.3 months (range, 0-6.5). Of the patients who experienced hemorrhage, 71% had complete resolution and 11% had partial resolution (defined as a decrease in severity by one or more grades from the worst grade) at last follow-up.

Monitor patients for signs and symptoms of hemorrhage. For patients experiencing pulmonary or CNS hemorrhage, permanently discontinue TIVDAK. For grade ≥2 hemorrhage in any other location, withhold until bleeding has resolved, blood hemoglobin is stable, there is no bleeding diathesis that could increase the risk of continuing therapy, and there is no anatomical or pathologic condition that can increase the risk of hemorrhage recurrence. After resolution, either resume treatment or permanently discontinue TIVDAK.

### Pneumonitis

Severe, life-threatening, or fatal pneumonitis can occur in patients treated with antibody drug conjugates containing vedotin including TIVDAK. Among patients with cervical cancer treated with TIVDAK across clinical trials, 2 patients (1.3%) experienced pneumonitis, including 1 patient who had a fatal outcome.

Monitor patients for pulmonary symptoms indicative of pneumonitis. Symptoms may include hypoxia, cough, dyspnea or interstitial infiltrates on radiologic exams. Infectious, neoplastic, and other causes for such symptoms should be excluded through appropriate investigations.

Withhold TIVDAK for patients who develop persistent or recurrent Grade 2 pneumonitis and consider dose reduction. Permanently discontinue TIVDAK in all patients with Grade 3 or 4 pneumonitis.

### Embryo-Fetal Toxicity

Based on the mechanism of action and findings in animals, TIVDAK can cause fetal harm when administered to a pregnant woman.

The small molecule component of TIVDAK, monomethyl auristatin E (MMAE), administered to rats caused adverse developmental outcomes, including embryo-fetal mortality and structural abnormalities, at exposures below those occurring clinically at the recommended dose.

Advise patients of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TIVDAK and for 2 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TIVDAK and for 4 months after the last dose.

## ADVERSE REACTIONS

### 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 TIVDAK in 158 patients with recurrent or metastatic cervical cancer who received at least one dose of TIVDAK at 2 mg/kg intravenously every 3 weeks in innovaTV 204 (NCT03438396), innovaTV 201 (NCT02001623), innovaTV 202 (NCT02552121) and innovaTV 203 (NCT03245736).

The data described in this section reflect exposure to TIVDAK from innovaTV 204 (NCT0348396), a single arm study in patients (n=101) with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. Patients received TIVDAK 2.0 mg/kg every 3 weeks until disease progression or unacceptable toxicity. The median duration of treatment was 4.2 months (range: 0.7-16).

Serious adverse reactions occurred in 43% of patients. The most common (≥3%) serious adverse reactions were ileus (6%), hemorrhage (5%), pneumonia (4%), peripheral neuropathy, sepsis, constipation, and pyrexia (each 3%). Fatal adverse reactions occurred in 4% of patients who received TIVDAK, including septic shock (1%), pneumonitis (1%), sudden death (1%), and multisystem organ failure (1%).

Adverse reactions leading to permanent discontinuation occurred in 13% of patients receiving TIVDAK; the most common (≥3%) adverse reactions leading to permanent discontinuation were peripheral neuropathy (5%) and corneal adverse reactions (4%).

Adverse reactions leading to dose interruption occurred in 47% of patients; the most (≥3%) common adverse reactions leading to dose interruption were peripheral neuropathy (8%), conjunctival adverse reactions (4%), and hemorrhage (4%).

Adverse reactions leading to dose reduction occurred in 23% of patients; the most common (≥3%) adverse reactions leading to dose reduction were conjunctival adverse reactions (9%) and corneal adverse reactions (8%).

The most common (≥25%) adverse reactions, including laboratory abnormalities, were hemoglobin decreased, fatigue, lymphocytes decreased, nausea, peripheral neuropathy, alopecia, epistaxis, conjunctival adverse reactions, hemorrhage, leukocytes decreased, creatinine increased, dry eye, prothrombin international normalized ratio increased, activated partial thromboplastin time prolonged, diarrhea, and rash.

**Table 4: Adverse Reactions (≥10%) in Patients Who Received TIVDAK in innovaTV 204**

| Adverse Reaction | TIVDAK N=101 | |
|---|---|---|
| | All Grades % | Grade 3-4 % |
| **General** | | |
| Fatigue[1] | 50 | 7 |
| Pyrexia | 16 | 1 |
| Pruritus | 13 | 1 |
| **Gastrointestinal disorders** | | |
| Nausea[2] | 41 | 0 |
| Diarrhea[3] | 25 | 2 |
| Constipation | 23 | 2 |
| Abdominal Pain[4] | 23 | 1 |
| Vomiting | 17 | 2 |
| **Nervous system disorders** | | |
| Peripheral Neuropathy[5] | 39 | 7 |
| **Skin and subcutaneous tissue disorders** | | |
| Alopecia | 39 | 0 |
| Rash[6] | 25 | 0 |
| **Vascular disorders** | | |
| Epistaxis | 39 | 0 |
| Hemorrhage[7] | 32 | 6 |
| **Eye disorders** | | |
| Conjunctival adverse reactions[8] | 37 | 0 |
| Dry eye[9] | 29 | 0 |
| Corneal adverse reactions [10] | 21 | 3 |
| Periorbital adverse reactions[11] | 16 | 0 |
| **Musculoskeletal and connective tissue disorders** | | |
| Myalgia[12] | 21 | 0 |
| Arthralgia | 16 | 0 |
| Pain in extremity[13] | 13 | 1 |
| **Metabolism and nutrition disorders** | | |
| Decreased appetite | 16 | 1 |
| **Infections** | | |
| Urinary tract infection[14] | 14 | 2 |
| **Investigations** | | |
| Weight decreased | 12 | 0 |

1. Fatigue includes fatigue and asthenia
2. Nausea includes nausea and retching
3. Diarrhea includes diarrhea, gastroenteritis, and colitis
4. Abdominal pain includes abdominal pain, abdominal pain upper, abdominal pain lower, abdominal distention and abdominal discomfort
5. Peripheral neuropathy includes neuropathy peripheral, peripheral sensorimotor neuropathy, polyneuropathy, peripheral sensory neuropathy, paresthesia, hypoesthesia, burning sensation, neuralgia, sensory loss, peripheral motor neuropathy, muscular weakness, gait disturbance, and hyperesthesia
6. Rash includes rash, rash maculo-papular, rash macular, dermatitis acneiform, dermatitis allergic, and erythema
7. Hemorrhage includes vaginal hemorrhage, hematuria, rectal hemorrhage, cystitis hemorrhagic, lower gastrointestinal hemorrhage, urinary bladder hemorrhage, hematochezia, anal hemorrhage, gingival bleeding, post procedural hemorrhage, radiation associated with hemorrhage, metrorrhagia, large intestinal hemorrhage, paranasal sinus hemorrhage, and hemoptysis
8. Conjunctival adverse reactions includes conjunctivitis, conjunctival abrasion, conjunctival erosion, conjunctival hyperemia, conjunctival scar, noninfective conjunctivitis, ocular hyperemia, and conjunctival hemorrhage
9. Dry eye includes dry eye and lacrimation increased
10. Corneal adverse reactions includes keratitis, punctate keratitis, ulcerative keratitis, corneal erosion, corneal scar, keratopathy, and corneal bleeding

**continuation of Table 4 from previous page**

11. Periorbital adverse reactions includes blepharitis, meibomianitis, eye pruritus, entropion, trichiasis, chalazion, and meibomian gland dysfunction
12. Myalgia includes myalgia, musculoskeletal discomfort, and musculoskeletal pain
13. Pain in extremity includes pain in extremity and limb discomfort
14. Urinary tract infection includes urinary tract infection, urinary tract infection bacterial, and cystitis

Clinically relevant adverse reactions in <10% of patients who received TIVDAK in innovaTV 204 included venous thrombosis (3%), pulmonary embolism (3%), and pneumonitis (2%).

**Immunogenicity**

As with all therapeutic proteins, there is potential for an immune response to TIVDAK. The detection of antibody formation against tisotumab vedotin-tftv is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to tisotumab vedotin-tftv in other studies or to other products may be misleading.

In innovaTV 204, a total of 93 patients were tested for immunogenicity to TIVDAK; 5 patients (5%) developed treatment-emergent anti-tisotumab vedotin-tftv antibodies. Neutralizing anti-tisotumab vedotin-tftv antibodies were detected in 2 patients in Study innovaTV 204. Across all studies, 8 cervical cancer patients (5.5%) out of 145 evaluable patients developed treatment-emergent anti-tisotumab vedotin-tftv antibodies. Given the low number of patients who developed anti-tisotumab vedotin-tftv antibodies, no conclusions can be drawn concerning a potential effect of immunogenicity on PK, efficacy or safety.

**DRUG INTERACTIONS**

**Effects of Other Drugs on TIVDAK**

Strong CYP3A4 Inhibitors

MMAE is a CYP3A4 substrate. Concomitant use of TIVDAK with strong CYP3A4 inhibitors may increase unconjugated MMAE exposure, which may increase the risk of TIVDAK adverse reactions. Closely monitor patients for adverse reactions of TIVDAK when used concomitantly with strong CYP3A4 inhibitors.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

Risk Summary

Based on the mechanism of action and findings in animals, TIVDAK can cause fetal harm when administered to a pregnant woman. There are no available human data on TIVDAK use in pregnant women to inform a drug-associated risk. In an animal reproduction study, administration of the small molecule component of TIVDAK, MMAE, to pregnant rats during organogenesis caused embryo-fetal mortality and structural abnormalities at exposures below the clinical exposure at the recommended dose (see Data). Advise patients 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%-4% and 15%-20%, respectively.

Data

*Animal Data*

No embryo-fetal development studies in animals have been performed with tisotumab vedotin-tftv. In an embryo-fetal development study in pregnant rats, administration of two intravenous doses of MMAE, the small molecule component of TIVDAK, on gestational days 6 and 13 caused embryo-fetal mortality and structural abnormalities, including protruding tongue, malrotated limbs, gastroschisis, and agnathia compared to controls at a dose of 0.2 mg/kg (approximately 0.5-fold the human area under the curve [AUC] at the recommended dose).

**Lactation**

Risk Summary

There are no data on the presence of tisotumab vedotin-tftv 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 lactating women not to breastfeed during treatment with TIVDAK and for at least 3 weeks after the last dose.

**Females and Males of Reproductive Potential**

TIVDAK can cause fetal harm when administered to a pregnant woman.

Pregnancy testing

Verify pregnancy status in females of reproductive potential prior to initiating TIVDAK treatment.

Contraception

*Females*

Advise females of reproductive potential to use effective contraception during treatment with TIVDAK and for 2 months after the last dose.

*Males*

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TIVDAK and for 4 months after the last dose.

Infertility

*Males*

Based on findings from animal studies, TIVDAK may impair male fertility.

**Pediatric Use**

Safety and effectiveness of TIVDAK in pediatric patients have not been established.

**Geriatric Use**

Of the 101 patients treated with TIVDAK in innovaTV 204, 13% were ≥65 years of age. Grade ≥3 reactions occurred in 69% patients ≥65 years and in 59% patients <65 years. Serious adverse reactions occurred in 54% patients ≥65 years and in 41% patients <65 years. No patients aged ≥65 years treated with TIVDAK in innovaTV 204 experienced a tumor response.

**Hepatic Impairment**

Avoid use of TIVDAK in patients with moderate or severe hepatic impairment (total bilirubin > 1.5 × ULN)

In patients with mild hepatic impairment (total bilirubin ≤ ULN and AST >ULN or total bilirubin > 1 to 1.5 × ULN and any AST), closely monitor patients for adverse reactions of TIVDAK, but no dosage adjustment in the starting dose of TIVDAK is recommended.

**Please see the full Prescribing Information, including BOXED WARNING, at tivdakhcp.com**

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