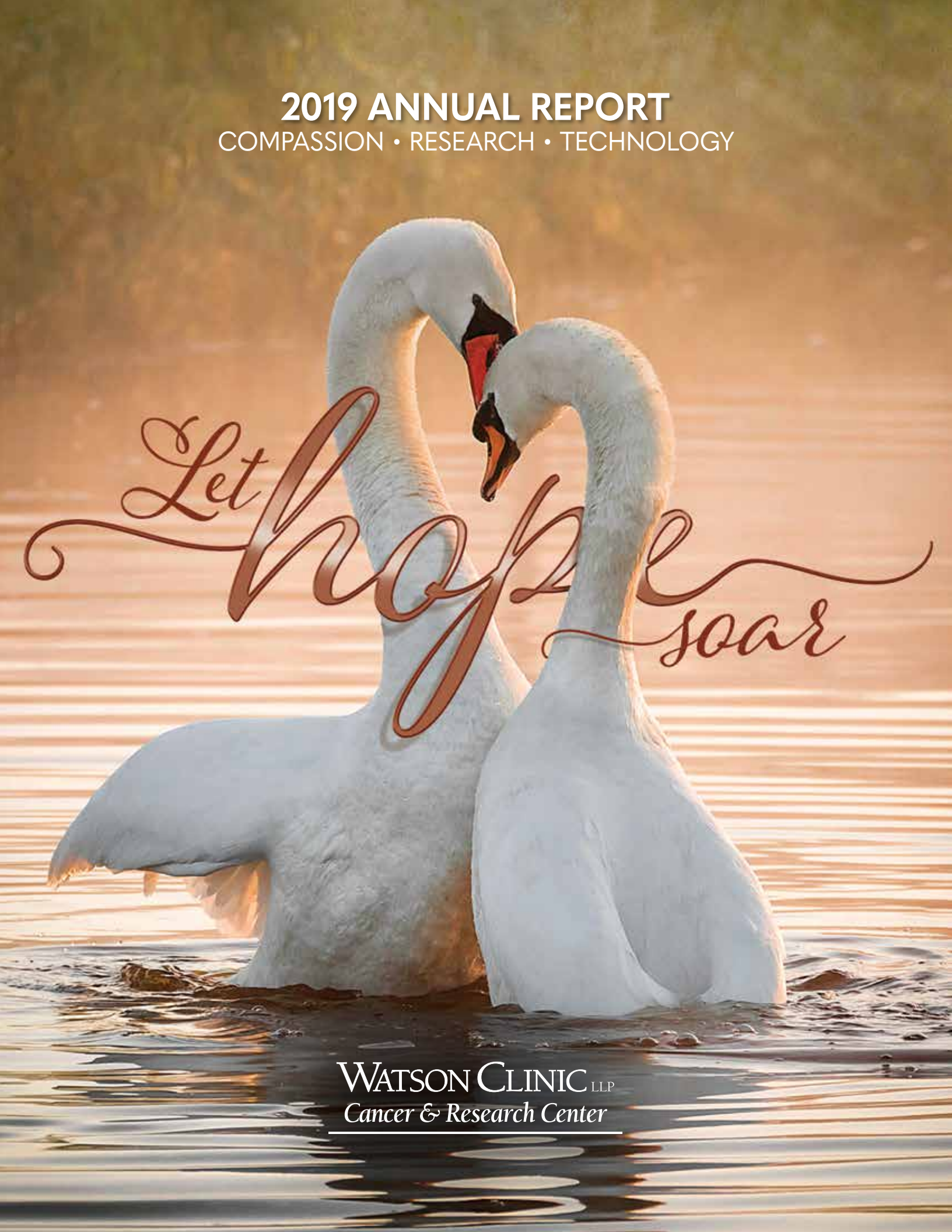
2019 ANNUAL REPORT

COMPASSION • RESEARCH • TECHNOLOGY



WATSON CLINIC LLP

Cancer & Research Center

Table of Contents

HOPE is perhaps the most meaningful service provided by the specialists and assorted care team members at the Watson Clinic Cancer & Research Center. More than medicines, treatments or technologies, the power of hope can elevate the spirit and determination of patients who are in the battle of their lives.

As we enter our 17th year of operation, we take the most pride in serving as a reliable partner in hope for every patient, family member and caregiver we encounter.

Hope in cancer care originates from the belief that survivorship is possible, and this often begins with the confidence a patient feels in the team they chose to fight by their side.

We've built a rock-solid reputation for innovation and personalization that spreads far beyond the confines of our community. For these efforts, we've earned full accreditation from the American College of Surgeons Commission on Cancer, and were named Florida's sole recipient of their Outstanding Achievement Award in both 2013 and 2016.

Our world class multi-disciplinary team includes experts in fields like oncology-hematology, surgical oncology, and gynecologic and urologic oncology. They work together to formulate the most effective plans of action for each patient, and they utilize the most progressive technologies and research protocols to target and destroy invading cancers. When ancillary care is required as a compliment to these primary courses of treatment, our patients enjoy swift referrals to Watson Clinic's extended family of more than 220 board-certified physicians in disciplines that range from primary care, gastroenterology, podiatry and plastic & reconstructive surgery. Additional support comes from our team of social workers, nurse navigators and other staffers who work to eliminate any practical obstacles that stand between the patient and their full recovery.

We witness the power of hope in our everyday encounters with patients and families who remain vigilant and united in the face of great hardship. All of us at the Watson Clinic Cancer & Research Center consider it our sacred responsibility to create an environment where that hopeful spirit can soar.

A MESSAGE FROM
Shalini Mulaparthi, MD
CANCER COMMITTEE CHAIR

We are Polk, we are Watson, mostly we are here to care. We care about the 1000's of people who trust us year round with their lives. They are our people, not just patients. Each person has their own unique story with challenges and victories. We are committed to serving them with compassion, care and great respect.

Cancer is one of the world's most pressing healthcare challenges, with more than 14 million people receiving a cancer diagnosis each year. Thanks to investment and progress in cancer research, people today are living longer with this disease than ever before.

Precision medicine, molecular testing and diagnosis, Immunotherapy advances, new successes with targeted therapies, and growing micro biome research are just a few major advances we have achieved in 2019 in the field of cancer research.

There were approximately 1,500 newly diagnosed cancer patients seen at Watson Clinic in 2019. Out of those treated at the cancer center, 285 were breast cancer diagnosis, 76 were colorectal and 170 were lung cancer.

We have also identified areas on which future research efforts should be focused to help accelerate progress against cancer. Some of our priorities are listed here:

1. **Identify strategies that better predict response to immunotherapies.**
2. **Better define the patient populations that benefit from postoperative (adjuvant) therapy.**
3. **Translate innovations in cellular therapies to solid tumors.**
4. **Increase equitable access to cancer clinical trials.**
5. **Reduce the long-term consequences of cancer treatment.**

I am incredibly encouraged by the growth of our cancer center year over year. Our mission always has been and will continue to be pursuing the latest discoveries in cancer care and delivering the best possible care for our patients.

A MESSAGE FROM

Galina Vugman, MD

CANCER LIAISON PHYSICIAN

Every day, people choose Watson Clinic for cancer treatment. It continues to be my privilege to serve as the Cancer Liaison Physician at Watson Clinic.

How will the cures for cancer be found? The answer is research. With continued support, we will continue to foster collaboration in our area. We are proud to have partnered with UF Health to accelerate and broaden the availability of new research in our community.

Cancer is a disease which has touched many people whether it is a personal diagnosis or that of a loved one or of a friend. So far in 2019, the FDA have approved numerous new therapies for hematologic and solid tumors.

"Cancer begins and ends with people. In the midst of scientific abstraction, it is sometimes possible to forget this one basic fact..." – *Siddhartha Mukherjee, The Emperor of All Maladies*

To take care of cancer patients is an enormous privilege. I thank you for the trust you put in us on a daily basis.

Center for Research

The Watson Clinic Center for Research, Inc. Oncology department has opened some exciting trials during 2019, and has enrolled many patients with various cancer diagnoses. Our multidisciplinary team comprised of medical oncologists, surgical oncologists, radiation oncologists, interventional radiologists, urologists, pulmonologists, otolaryngologists, pathologists and radiologists has explored new trials in the following cancer diagnoses: breast, lung, lymphoma, myelodysplastic syndromes, acute myeloid leukemia and renal.

This year we established an NRG Oncology affiliation with the University of Florida. NRG Oncology is a non-profit research organization formed to conduct oncologic clinical research and to broadly distribute study results for informing clinical decision making and healthcare policy. It brings together the National Surgical Adjuvant Breast and Bowel Project (NSABP), Radiation Therapy Oncology Group (RTOG), and the Gynecologic Oncology Group (GOG) — each recognized internationally as a research leader. NRG Oncology embodies an impressive legacy in the conduct of multi-institutional phase II and phase III clinical trials. This affiliation has brought new exciting and promising scientific trials to our community. The University of Florida and Watson Clinic Center for Research have mutual interest in the advancement of medical research in cancer-related fields and anticipate collaborative research arising from this relationship.

Many of our current multicenter trials are studying how new treatment oncology regimens improve survival and provide better quality of life for our cancer patients. Every day, patients seen in the clinic and hospital are screened to determine if they are eligible for an available trial. Twice weekly our research team takes part in Tumor Board Conferences to explore research options for treatment decisions relevant to individual patient care. Our research investigators and coordinators meet regularly to evaluate new potential trials and determine feasibility of conducting this trial in our community.

In addition, the research team conducted breast cancer educational retreats for college-age students at four colleges and universities in Polk County during 2019 through a Florida Breast Cancer Foundation Grant.

These activities help us to continue to be an integral part of cancer care for our patients in the community. Through education and research we are continuing to offer new promising cancer treatments and improve patient cancer outcomes through evidence based medicine.

Cancer Conferences

WATSON CLINIC CANCER & RESEARCH CENTER – 2018 AND 2019

Cancer conferences not only serve as a forum for prospective review of cancer cases involving a multidisciplinary team in the patient care process, but also offers education for the physicians and care team members. Our multidisciplinary team includes physicians in the departments of medical oncology-hematology, radiation oncology, surgical oncology, pathology, diagnostic radiology, and other specialties, as well as allied health professionals from research, nursing, social services, cancer registry and administration. They attend cancer conferences three times a week for collaborative discussions of diagnosis, stage, prognostic factors, and national treatment guidelines pertaining to the cases presented and cancer related educational activities.

CANCER CONFERENCES YEAR END 2018

Total # of Cancer Conferences:

95

Total # of Cancer Related Educational Activities:

24

Total # of Cases Presented:

821 — 91% of Analytic Caseload

Total # of Cases Presented Prospectively:

821 — 100% of Cases Presented

CANCER CONFERENCES JAN. 1, 2019 – SEPT. 30, 2019

Total # of Cancer Conferences:

71

Total # of Cancer Related Educational Activities:

21

Total # of Cases Presented:

563 — 63% of Analytic Caseload

Total # of Cases Presented Prospectively:

563 — 100% of Cases Presented

Cancer Committee Members 2019

PHYSICIAN MEMBERS

Dr. Elisabeth Dupont, Breast Surgery
Dr. Edward Garcia, Pathology
Dr. Howard Gorell, Radiology
Dr. Thomas Moskal, Surgical Oncology
Dr. Shalini Mulaparthi, Medical Oncology/Hematology, Cancer Committee Chair
Dr. Sandra Sha, Radiation Oncology
Dr. Galina Vugman, Medical Oncology/Hematology, Cancer Liaison Physician

PHYSICIAN-ASSOCIATE MEMBERS

Dr. Richard Cardosi, Gynecologic Oncology
Dr. Tim Dickason, Pathology
Dr. Randy Heysek, Radiation Oncology
Dr. Scott Kelley, Surgery
Dr. David Lowry, Radiology
Dr. Neeharika S. Makani, Oncology/Hematology
Dr. Jack Thigpen, Surgery

ACTIVITY COORDINATORS

Peggy Garrett, Program Coordinator Watson Clinic Foundation, Community Outreach
Cindy Bruton, Sr. Administrative Assistant, Cancer Conference
Monique Hakins, MSW, Social Services, Psychosocial Services
Jennifer Snider, CTR, Cancer Program Coordinator & Quality Control
Noreen McGowan, BSN, CCRC, Director, Clinical Research
Debra Hemm, RN, OCN, Chemotherapy/Oncology Nurse Navigator, Quality Improvement

NON-PHYSICIAN MEMBERS

Mashell Hooker, RN, OCN, Chemotherapy Charge Nurse
Jerri Huntt, MSW, LCSW, Women's Center Social Services
Aiman Kumha, MBA, Director Clinical Services
Carol Martin, RN, Women's Center Clinical Services Coordinator
Shirley Willis, RN, MSN, Cancer Center Clinical Services Coordinator
Jie Yang, PhD, DABR, Radiation Physicist
Sonia Wellinger, Chief Operating Officer
Stephanie McLean, American Cancer Society Area Patient Representative

Head and Neck Cancer: An Analysis of the Impact of HPV Status and Smoking History on Patient Outcomes

MADELINE PISTORIA AND NITESH PARYANI, MD

INTRODUCTION

In the United States, oropharyngeal squamous cell carcinoma (OSCC) is the eighth most common cancer among men and the fourteenth most common among women. Historically, approximately 75% of all oral squamous cell carcinomas were a result of tobacco use.[1] Although the prevalence of tobacco associated oral cavity cancers has decreased likely due to the overall decline in tobacco use, the occurrence of human papillomavirus (HPV) linked oropharyngeal cancers has increased. HPV has been classified as an inducing agent for head and neck cancers, especially those located in the oropharynx.[1] HPV is a common sexually transmitted disease that is thought to be the leading cause in the majority of oropharyngeal cancers today.[2] The prevalence of HPV-positive oropharynx tumors has increased dramatically over the past couple of decades, suggesting HPV's principal role in the recent increase. Oropharyngeal cancers that are HPV-driven, specifically HPV-positive, have been shown to have a considerably higher survival rate than those derived from a history of tobacco use.[3] The difference in treatment outcomes for head and neck cancer patients based on their HPV status as well as the underlying importance of HPV testing will need to be thoroughly evaluated to further understand their association.

METHODOLOGY

The Watson Clinic Cancer & Research Center Cancer Registry provided a list of seventy-eight patients diagnosed with OSCC during the timeframe of January 1, 2013 to December 31, 2017. The participants of the study have undergone combined chemotherapy and radiation therapy. Specific data was reviewed regarding each patient's diagnosis by utilizing Watson Clinic's medical records and Lakeland Regional's hospital records. A chart review involved the collection of the following data: patient gender, patient age, dates treated, HPV status, tumor stage, radiation fraction and dose, chemotherapy regimen, imaging findings, endoscopy findings, and clinical outcome. P-16, a tumor suppressor protein is commonly and highly correlated with HPV and was used as the determining factor in the patients' HPV status. Because roughly one-third of the patients had an unknown HPV status, the smoking history of the patient was abstracted. Once collected, HPV-positive patients' records were abstracted to see if the expected clinical outcome occurred.

RESULTS

This study has been divided into two intertwined components, those tested for HPV and those who were not tested. The patients whose HPV statuses were unavailable were separated into two groups, smokers and nonsmokers.

While retrieving data, a total of 55 (70%) of the original 78 patients had been tested for HPV. Of these, 85.45% were HPV-positive and approximately 72.34% of the HPV-positive patients were alive without disease. Less than 20% of those tested for HPV continue to live with the disease or died due to the disease.

The patients who were not tested for HPV were further divided by individual smoking history. A majority of the patients had a smoking history (78.26%) and 50% were alive without disease.

Patient Demographics

AGE	
Mean	63.6
Median	64
Range	33-87
GENDER	
Male	63 (81%)
Female	15 (19%)

Figure 1: n = 78

Of those who had no past smoking history (21.74%) only one patient had died as a result of the disease.

Of the total 78 patients, 65% are alive without disease and only 20% either passed away as a result of OSCC or are currently living with the disease.

Comparison of HPV Status and Smoking Status Clinical Outcomes

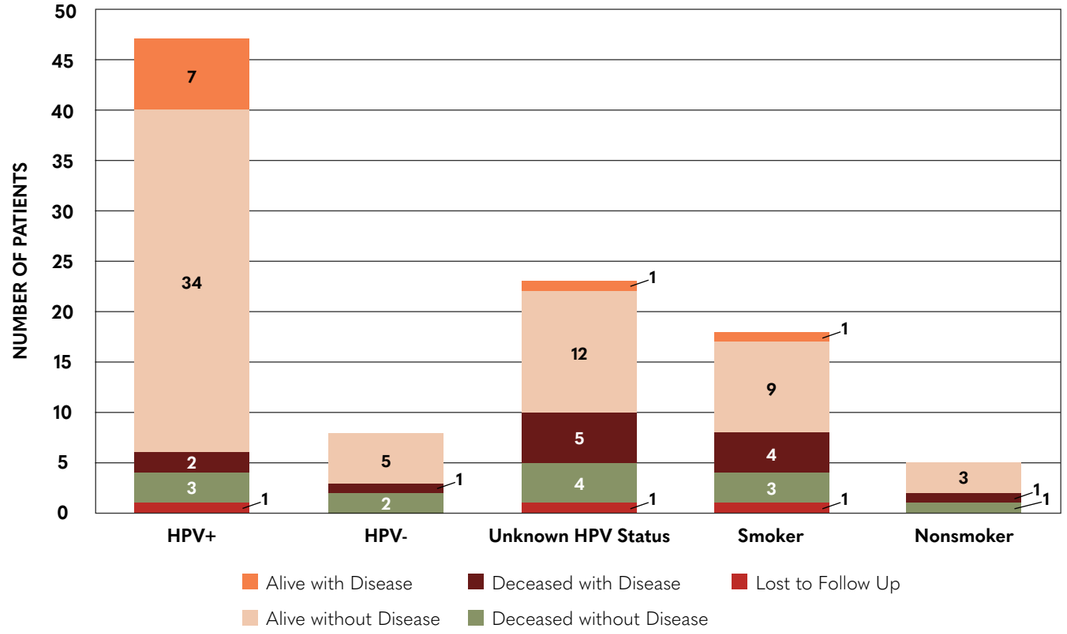
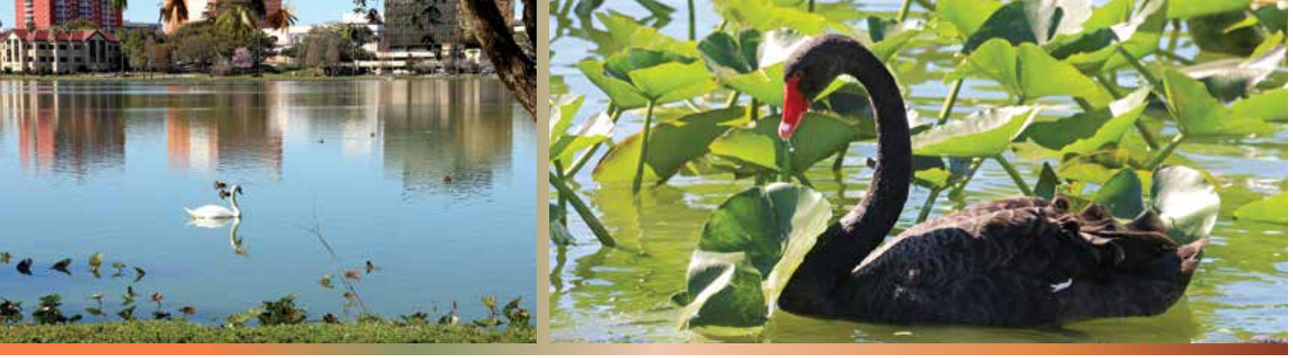


Figure 2: Comparison of the clinical outcomes those HPV-positive, HPV-negative, smokers, and nonsmokers. n=78



DISCUSSION

There is growing evidence that there are better treatment outcomes for oropharyngeal squamous cell carcinoma patients who are HPV-positive. A laboratory can sample biopsied tissue to determine a positive p-16 status of an OSCC, increasing the likelihood of a positive HPV status.[4] In this study, not all of the patients were tested for HPV, making data collection difficult. Some charts stated the intention of HPV testing, but there was a lack of documentation of said testing and follow-up. The smoking histories were abstracted from the charts to compensate for the missing HPV status. While this information did not fully help determine whether HPV status affects clinical outcome, it did help give insight into the clinical outcomes of patients with a history of smoking.

Overall, those HPV-positive patients had a non-statistically significant better prognosis for OSCC free survival. There are ongoing studies that are seeking to determine whether HPV-positive cancers can undergo less-intensive treatments and still have a high survival rate.[3, 5]

CONCLUSION

This study has taken efforts to help determine if HPV status can make a difference in clinical outcome. According to previous studies, patients that are HPV-positive have a higher survival rate for oropharyngeal squamous cell carcinomas than those that are HPV-negative. The statistics from the data abstraction indicate that out of the original 78 patients, 43.59% were HPV-positive and are living OSCC free. These patients had a higher chance of survival than those who were former smokers and had an even greater chance of survival compared to HPV-negative patients. The lack of HPV testing has proven to be a problem while conducting this. With 30% of patients without a HPV status, it has become evident that there is need for improvement in testing for HPV in head and neck cancers. Knowledge of the patient's HPV status will help guide providers in their discussions with patients regarding risks and benefits of treatment, as well as expected outcomes. In an effort to fully understand the differences between human papillomavirus status and oropharyngeal squamous cell carcinomas, more research should be conducted using a larger number of patients with a known HPV status.

REFERENCES

1. Chaturvedi, A. K.; Engels, E. A.; Anderson, W. F.; Gillison, M. L. Incidence Trends for Human Papillomavirus – Related and – Unrelated Oral Squamous Cell Carcinomas in the United States. *Journal of Clinical Oncology* 2008, *26* (4), 612–619.
2. HPV and Oropharyngeal Cancer | CDC. https://www.cdc.gov/cancer/hpv/basic_info/ hpv_oropharyngeal.htm (accessed Jul 1, 2019).
3. Mirghani, H.; Blanchard, P. Treatment De-Escalation for HPV-Driven Oropharyngeal Cancer: Where Do We Stand? *Clinical and Translational Radiation Oncology* 2018, *8*, 4–11.
4. Sturgis, E. M.; Ang, K. K. The Epidemic of HPV-Associated Oropharyngeal Cancer Is Here: Is It Time to Change Our Treatment Paradigms? *Journal of the National Comprehensive Cancer Network* 2011, *9* (6), 665–673.
5. Nguyen-Tan, P.; Zhang, E.; Wheeler, R.; Weber, R.; Rosenthal, D.; Vigneault, E.; Kim, H.; Silverman, C.; Raben, A.; Ang, K. A Phase 3 Trial to Test Accelerated Versus Standard Fractionation in Combination With Concurrent Cisplatin for Head and Neck Carcinomas (RTOG 0129): Long-Term Report of Efficacy and Toxicity. *International Journal of Radiation Oncology*Biology*Physics* 2014, *87* (2).

Quality Outcomes in Colon Cancer

MICHELLE MOSKAL AND
NEEHARIKA MAKANI, MD

INTRODUCTION

In the United States, colon cancer is the second leading cause of cancer-related deaths among men and women combined. There is a 4-5% lifetime risk of developing colorectal cancer. In 2019, it has been estimated that 140,250 new cases of colon cancer will be diagnosed and approximately 51,020 deaths are expected from colon cancer.[8, 18]

There has been a decline in the death rate associated with colorectal cancer. This has been attributed to early detection of pre-cancerous polyps with routine screening colonoscopy. Additionally, there has been improvement in treatment of colorectal cancers. Thus there are now more than one million survivors of colorectal cancer in the United States.[18]

Current treatment of colorectal cancer is dictated by the stage of the cancer. There are a series of tests and procedures that are performed at the time of diagnosis to accurately stage the cancer. Initial work up for colon cancers includes colonoscopy, imaging such as CT or MRI and blood tests. Most patients with non-metastatic colon cancer will have surgery. Following surgery, patients need further blood tests, and some will need chemotherapy.[4, 10, 11]

PURPOSE

A retrospective review of Watson Clinic patients with non-metastatic, early stage colon cancer was performed to determine if they received appropriate preoperative evaluation and adequate postoperative management based on stage of the disease using the National Comprehensive Cancer Network (NCCN) as a benchmark.

PATIENTS AND METHODS

A retrospective study was initiated to assess the adherence of pre and postoperative management of non-metastatic colon cancer patients to current national guidelines. A query of the Watson Clinic Cancer & Research Center Cancer Registry was completed to provide the list of patients diagnosed with stage II and III colon cancer who had been treated at the Watson Clinic Cancer & Research Center between 1/1/2015 – 12/31/2018. The medical records of 104 patients treated during the study period with the biopsy-proven diagnosis of stage II and III colon cancer were reviewed retrospectively.

The NCCN defines stage II colon cancer as cancer that has grown into, or beyond, the fourth layer of the colon wall without the presence of cancer in nearby lymph nodes or areas distant from the colon. Stage III colon cancer has spread from the colon to nearby lymph nodes and/or there is the presence of tumor deposits. Patients with stage II colon cancer were further subdivided into low and high risk categories on the basis of criteria defined by both the American Society of Clinical Oncology (ASCO) and NCCN guidelines: fewer than 12 lymph nodes in the surgical specimen, T4 or perforated/obstructed lesion, lymphovascular or perineural invasion, poorly differentiated histology (signet ring or mucinous cell), and mismatch repair proficient (pMMR) or microsatellite instability (MSI) low.[4, 10, 11]

This study defined adherence to guidelines based on whether adequate surgical resection was administered to the patient and if appropriate adjuvant chemotherapy was offered. Patients treated in accordance with these recommendations were categorized as “adherent,”

and those not treated in accordance with these recommendations were categorized as "nonadherent." Subsequently, nonadherence was categorized as either "overtreatment" or "under-treatment" (Figure 1).[2]

In order to determine if the differences in the data proportions were significant, an "N-1" Chi-squared test was used for comparison of proportions. The stage II low risk subdivision with 19 patients and stage II high risk subdivision with 27 patients were combined to create one group with a total of 46 patients. These stage II patients were compared to the proportions of the stage III cohort with 58 patients. This combination ensured a more equal sample size comparison of proportions. Additionally, a three-way analysis of variance (ANOVA) test was performed to determine the significance of pathology results between the three stratified, independent groups. The level of significance calculated was $p < 0.05$. Statistical analysis was not performed for patient demographics and characteristics as these factors were not being assessed for association with protocol adherence.

Figure 1: Stage-specific colon cancer treatments based on National Comprehensive Cancer Network (NCCN) guidelines.

Stage II Low Risk (T3, grade < 3, ≥ 12 nodes)	**Adherent**		Adequate surgical resection
	Nonadherent	**Overtreatment**	Adequate surgical resection + chemo/radiation
		Undertreatment	Inadequate surgical resection
Stage II High Risk (T4, grade ≥ 3, < 12 nodes)	**Adherent**		Adequate surgical resection + chemo
	Nonadherent	**Overtreatment**	Adequate surgical resection + chemo/radiation
		Undertreatment	Adequate surgical resection ± radiation
Stage III	**Adherent**		Adequate surgical resection + chemo
	Nonadherent	**Overtreatment**	Adequate surgical resection + chemo + radiation
		Undertreatment	Adequate surgical resection ± radiation

RESULTS

Patient Demographics and Baseline Characteristics

The gender distribution of patients did not differ across stages with 51.0% of overall patients being male and 49.0% of patients being female. The age ranged between 31 and 100. The majority of patients were in the age group of 61 to 80 years of age. Younger patients were more likely to present with stage II low risk disease (68.4% of stage II low risk patients were <70 years old). Across stages, the bulk of patients were Caucasian (91.3%) with smaller populations of African American (3.8%) or Hispanic (4.9%) descent. The average BMI of patients was 28.94 kg/m2. A family history of colon cancer was identified in 14.4% of the patient population. As a result of this family history of colon cancer in patients, further genetic testing and counseling was often conducted.

Preoperative Evaluation

Most cancers were identified through routine screening or incidental preoperative colonoscopy (77.9%) (Figure 2).

Figure 2: Identification of Colon Cancer

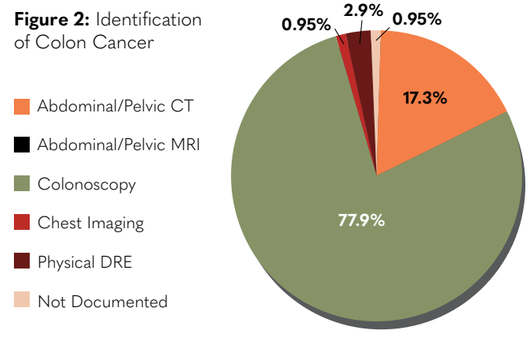


Table 1: Colonoscopy Findings Stratified by Cancer Stage

Characteristic	Percentage of Patients				
	Stage II Low Risk (n = 19)	Stage II High Risk (n = 27)	Stage III (n = 58)	P Value	Total (n = 104)
Histology					
Unspecified	19 (100.0%)	19 (70.4%)	50 (86.2%)	0.6151	88 (84.6%)
Mucinous	0	8 (29.6%)	6 (10.3%)	0.2941	14 (13.5%)
Medullary	0	0	0	-	0
Signet Ring Cell	0	0	2 (3.5%)	0.2022	2 (1.9%)
Size					
0-3	5 (26.3%)	6 (22.3%)	13 (22.4%)	0.8576	24 (23.1%)
3-5	9 (47.4%)	11 (40.7%)	16 (27.6%)	0.0921	36 (34.6%)
5-7	4 (21.1%)	8 (29.6%)	14 (24.1%)	0.8159	26 (25.0%)
≥7	0	1 (3.7%)	7 (12.1%)	0.0616	8 (7.7%)
Not Indicated	1 (5.2%)	1 (3.7%)	8 (13.8%)	-	10 (9.6%)
Polyp Removal					
Y	7 (36.8%)	19 (70.4%)	33 (56.9%)		59 (56.7%)
N	12 (63.2%)	8 (29.6%)	25 (43.1%)	0.3530	45 (43.3%)

There was no significant difference between histology across stages, with most cancers being unspecified adenocarcinomas (Table 1). Across stages, the largest proportion of patients had tumors ranging from 3-5 centimeters in size (34.6%).

Tests and procedures, such as comprehensive metabolic panels (CMP), complete blood counts (CBC), and the tumor marker carcinoembryonic antigen test (CEA), are typically performed at the time of diagnosis. CMP and CBC blood work were more likely to be performed across all stages. Only 55.8% of patients had CEA tested. Stage II low risk and stage II high risk patients were more likely to have a CMP and/or CBC tested than stage III patients (94.7% and 100.0% respectively as compared to 78.6% in stage III patients). A preoperative CEA test was less likely to be performed than any other test: 57.9% of stage II low risk patients, 35.7% of stage II high risk patients, and 48.2% of stage III patients. Abnormal CMP results were indicated in 89.4% of the cohort, abnormal CBC results in 85.6%, and abnormal CEA results in 63.5% of the patients who received each respective blood work, chemistry profile, and/or cancer marker (Figure 3). Additionally, imaging of the abdomen and pelvis with either CT scan (IV contrast) or MRI and chest imaging is performed preoperatively; however, it is acceptable to perform chest imaging studies postoperatively in patients with complicated colon cancers such as obstruction. Stage II high risk patients were more likely to receive abdominal and pelvic CT imaging by a slight margin (82.8%) as

Figure 3: Preoperative Laboratory Results for All Stages of Colon Cancer Patients (CMP, CBC, CEA)

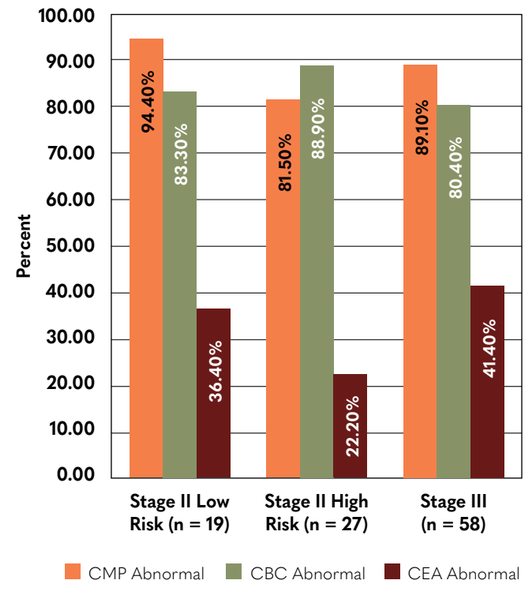


Table 2: Preoperative Evaluation Stratified by Cancer Stage

Characteristic	Percentage of Patients			
	Stage II Low Risk (n = 19)	Stage II High Risk (n = 27)	Stage III (n = 58)	Total (n = 104)
Labs				
CMP	18 (94.7%)	27 (100.0%)	46 (79.3%)	91 (87.5%)
CBC	18 (94.7%)	27 (100.0%)	46 (79.3%)	91 (87.5%)
CEA	11 (57.9%)	18 (66.7%)	29 (50.0%)	58 (55.8%)
Lab results				
CMP Normal	1 (5.5%)	5 (18.5%)	5 (10.9%)	11 (10.6%)
CBC Normal	3 (16.7%)	3 (11.1%)	9 (19.6%)	15 (14.4%)
CEA Normal	7 (63.6%)	14 (77.8%)	17 (58.6%)	38 (36.5%)
Imaging				
Abdominal/Pelvic CT	14 (73.7%)	22 (81.5%)	38 (65.5%)	74 (71.2%)
Abdominal/Pelvic MRI	1 (5.3%)	3 (11.1%)	2 (3.4%)	6 (5.8%)
Chest CT	3 (15.8%)	8 (29.6%)	11 (19.0%)	22 (21.2%)
Chest X-Ray	11 (57.9%)	11 (40.7%)	24 (41.4%)	46 (44.2%)

compared to stage II low risk (73.7%) and stage III patients (64.3%) (Table 2).

Adequate preoperative evaluation and management in colon cancer patients typically includes both blood work (labs) and imaging; however, some imaging may be performed postoperatively. 89.5% of stage II low risk patients in this study received both preoperative labs and imaging, while 5.25% of patients received neither. The highest compliance with these recommendations was exhibited by stage II high risk patients with 88.9% receiving both preoperative labs and imaging. 74.1% of stage III patients received both preoperative labs and imaging, while 15.5% of patients received neither (Figure 4).

Surgical Principles

Eighty percent of colon cancers are confined to the colon and/or regional lymph nodes. Surgery is currently the only curative treatment for localized colon cancer. The purpose of surgery is to remove the entire tumor along with the lymphatic drainage basin and the major vascular pedicle supplying blood to that colonic area. Across all stratified stages, the majority of surgeries received were right hemicolectomies (61.5%) (Figure 5).

Current national guidelines recommend that at least 12 lymph nodes be removed and evaluated for adequate staging.[3] All stage II low risk patients had 12

Figure 4: Preoperative Evaluation

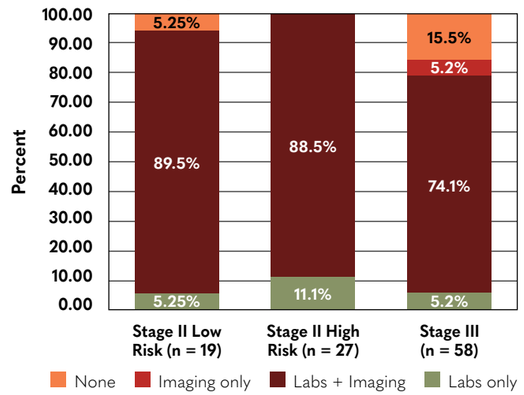
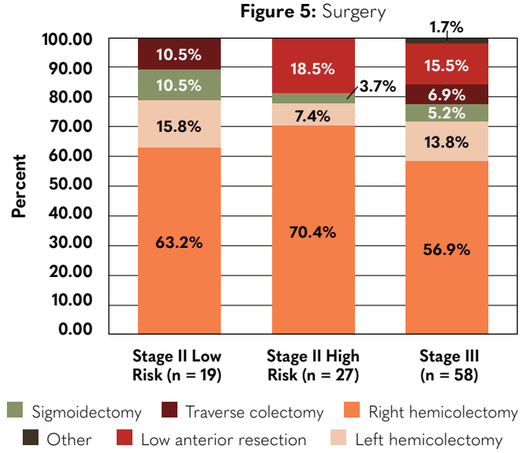
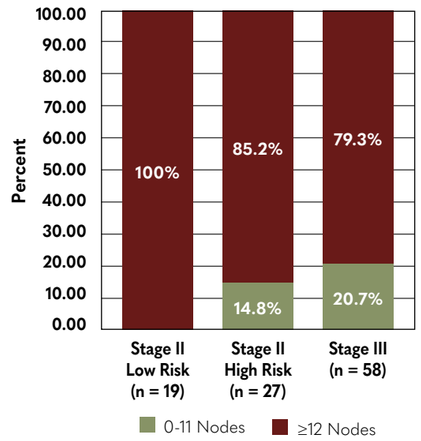


Figure 5: Surgery



or more lymph nodes removed and evaluated in accordance with national guidelines. Of the stage II high risk patients, 14.8% had less than the standard number of lymph nodes evaluated. Because these patients had less than the recommended 12 lymph nodes removed, they were categorized as high risk patients. In cases where fewer than 12 lymph nodes are removed, those patients are considered to be high risk for recurrence of colon cancer and are offered postoperative chemotherapy. 20.7% of stage III patients had less than 12 lymph nodes removed and evaluated (Figure 6).

Figure 6: Number of Lymph Nodes Evaluated



Principles of Pathology

When examining the final pathology results, a significant difference was calculated between stage II colon cancer patients and stage III colon cancer patients with grade one and grade three tumors (Table 3).

Table 3: Final Pathology Findings Stratified by Cancer Stage

Characteristic	Percentage of Patients				
	Stage II Low Risk (n = 19)	Stage II High Risk (n = 27)	Stage III (n = 58)	P Value	Total (n = 104)
Grade					
1	6 (31.6%)	5 (18.5%)	4 (6.9%)	0.0147	15 (14.4%)
2	13 (68.4%)	15 (55.6%)	32 (55.2%)	0.5608	60 (57.7%)
3	0	7 (25.9%)	19 (32.8%)	0.0405	26 (25.0%)
4	0	0	1 (1.7%)	0.3766	1 (1.0%)
Not indicated	0	0	2 (3.4%)	-	2 (1.9%)
Depth of Penetration					
Tis	0	0	0	-	0
T1	1 (5.3%)	0	1 (1.7%)	0.8543	2 (1.9%)
T2	2 (10.5%)	0	4 (6.9%)	0.5735	6 (5.8%)
T3	16 (84.2%)	27 (100.0%)	52 (89.7%)	0.4949	95 (91.3%)
T4	0	0	1 (1.7%)	0.3766	1 (1.0%)
Number of Lymph Nodes Positive					
0	18 (94.7%)	27 (100.0%)	3 (5.2%)	-	48 (46.2%)
1-3	0	0	37 (63.8%)	-	37 (35.6%)
4-7	0	0	12 (20.7%)	-	12 (11.5%)
>7	0	0	6 (10.3%)	-	6 (5.8%)
Not indicated	1 (5.3%)	0	0	-	1 (0.9%)
Status of Margins					
Positive	3 (15.8%)	2 (7.4%)	8 (13.8%)		13 (10.6%)
Negative	16 (84.2%)	25 (92.6%)	49 (84.5%)		90 (88.5%)
Not indicated	0	0	1 (1.7%)	0.8589	1 (0.9%)
Lymphovascular Invasion					
Y	0	7 (25.9%)	40 (69.0%)		47 (45.2%)
N	19 (100.0%)	19 (70.4%)	17 (29.3%)		55 (52.9%)
Not indicated	0	1 (3.7%)	1 (1.7%)	0.7853	2 (1.9%)
Perineural Invastion					
Y	0	0	12 (20.7%)		12 (11.5%)
N	19 (100.0%)	27 (100.0%)	44 (75.9%)		90 (86.5%)
Not indicated	0	0	2 (3.4%)	0.8748	2 (2.0%)
Tumor Deposits					
Y	0	0	9 (15.5%)	-	9 (8.7%)
N	19 (100.0%)	19 (100.0%)	46 (79.3%)	-	84 (88.5%)
Not indicated	0	0	3 (5.2%)	-	3 (2.8%)

57.7% of all patients had grade two tumors. No significant difference was calculated between the depth of penetration across cancer stages, with 91.3% of patients with T3 level of cancer. The number of positive lymph nodes was consistent with the definitions of colon cancer stages as none of the stage II low risk and stage II high risk patients presented with positive lymph nodes. 63.8% of stage III patients presented with between 1 and 3 positive lymph nodes from the evaluated surgical resection. 10.6% of patients had positive margins. Similarly, none of the stage II low risk and stage II high risk patients possessed tumor deposits, which was also consistent with the definition of the cancer stages from the NCCN. Lymphovascular invasion was seen in 69.0% of stage III patients and 25.9% of stage II high risk patients. Stage II low risk disease by definition cannot have lymphovascular and/or perineural invasion. Overall, 11.5% of patients – all from stage III – possessed perineural invasion (Table 3). Having perineural or lymphovascular invasion, increases the risk of colon cancer recurrence.

KRAS, NRAS, and/or BRAF mutation testing is recommended by the NCCN for patients presenting with colon cancer.[6] Overall, 90.4% of patients received KRAS testing. None of the patients in the study cohort received additional NRAS testing. About 5 to 9 out of every 100 people diagnosed with colon cancer have the BRAF V600E mutation, and as a result, this may explain why only 4.8% of patients received BRAF mutation testing[6] (Table 4).

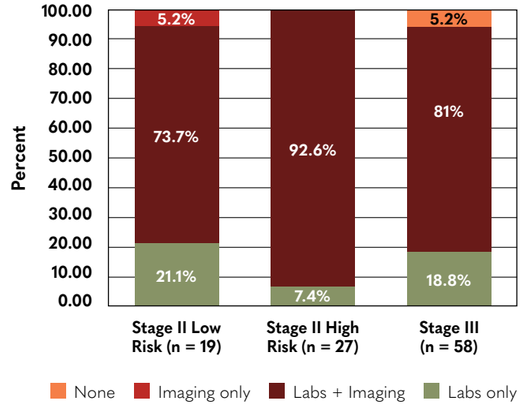
Table 4: Principles of Pathology Stratified by Cancer Stage

Characteristic	Percentage of Patients				
	Stage II Low Risk (n = 19)	Stage II High Risk (n = 27)	Stage III (n = 58)	P Value	Total (n = 104)
Mutation Testing KRAS NRAS BRAF	18 (94.7%) 0 0	23 (85.2%) 0 3 (11.1%)	53 (91.4%) 0 2 (3.4%)	0.6942 - 0.4635	94 (90.4%) 0 5 (4.8%)
Mutation Detected KRAS NRAS BRAF	6 (33.3%) 0 0	7 (30.4%) 0 2 (66.7%)	23 (43.4%) 0 2 (100.0%)	0.2497 - 0.4145	35 (33.7%) 0 4 (3.8%)

Postoperative Evaluation and Management

In evaluating postoperative management, the percentage of stage II low risk patients who received both labs, including CMP, CBC, CEA, and imaging, including abdominal/pelvic CT, abdominal/pelvic MRI, chest CT, and/or chest X-Ray, slightly decreased with comparisons of preoperative and postoperative evaluation and management (89.5% to 73.7%). The percentage of stage II high risk and stage III patients who received both labs and imaging slightly increased with comparisons of preoperative and postoperative evaluation and management (88.9% to 92.6% and 74.1% to 81.0% respectively) (Figure 7).

Figure 7: Postoperative Evaluation

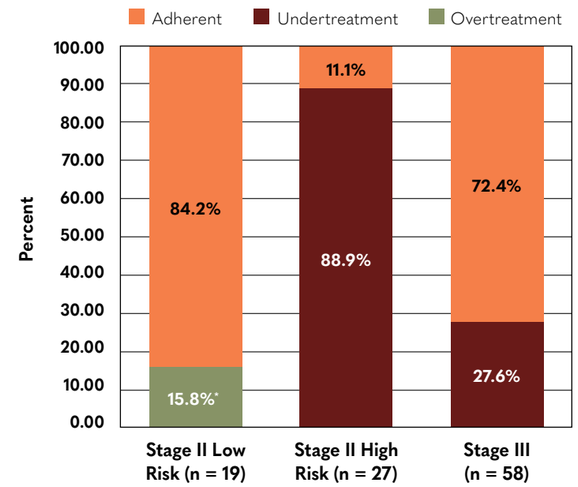


Adjuvant chemotherapy is defined as the administration of chemotherapy after surgery so as to reduce the risk of cancer recurrence based on stage of the disease and the presence of any high risk disease features. Patients with stage III colon cancer are often recommended adjuvant chemotherapy as there is a 30% reduction in the risk of disease recurrence and a 22-32% reduction in mortality. Additionally, postoperative chemotherapy is offered to stage II colon cancer patients considered to be high risk. The absolute benefit of chemotherapy for stage II high risk colon cancer is less compelling, with the absolute benefit of chemotherapy for overall survival being between 0-5%. Current NCCN guidelines recommend a 5-FU adjuvant chemotherapy regimen, which is to be initiated within 12 weeks of surgery.[9, 13] Of the stage III patients, 72.4% received adjuvant chemotherapy. Of the stage II high risk patients, only 11.1% of the patients actually received chemotherapy (Figure 8). A small percentage of stage II low risk patients were over-treated and given chemotherapy. As a result, 84.2% of stage II low risk patients were considered adherent. 11.1% of stage II high risk patients were considered adherent as a majority did not receive the recommended adjuvant chemotherapy. 72.4% of stage III patients were considered adherent according to the previously provided definitions (see "Patients and Methods").

The initiation of chemotherapy should be within 12 weeks of surgery. Overall, 97.9% of patients treated with adjuvant chemotherapy received treatment within 12 weeks after surgery. 100.0% of stage II patients received chemotherapy within the 12 weeks following surgery in both cohorts (Figure 9).

Postoperative radiation therapy in resected colon cancer is debated. Current treatment recommendations offer adjuvant radiation therapy to patients with T4b disease or a positive

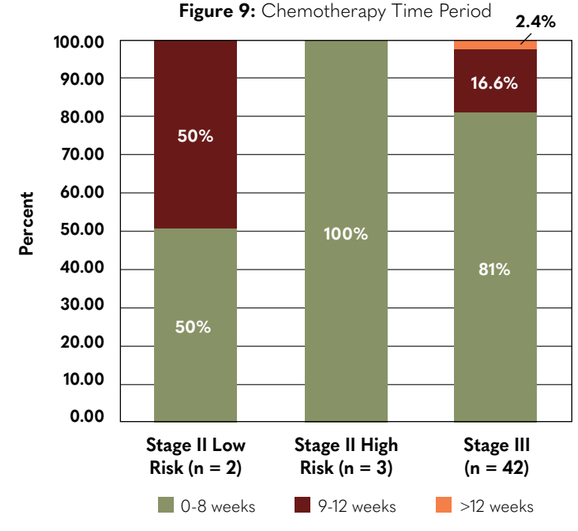
Figure 8: Chemotherapy and Treatment



Treatment	Stage II Low Risk	Stage II High Risk	Stage III
Adequate surgery only	16 (84.2%)	24 (88.9%)	16 (27.6%)
Adequate surgery + chemo	2 (10.5%)	3 (11.1%)	42 (72.4%)
Adequate surgery + radiation	1 (5.3%)	0 (0%)	0 (0%)

**The 15.8% of stage II low risk colon cancer patients possessed close surgical margins (a typical high risk feature).*

Figure 9: Chemotherapy Time Period



resection margin. One patient from the stage II low risk cohort received radiation therapy.

In cases where stage II high risk and stage III colon cancer patients did not receive adjuvant chemotherapy treatment, non-treatment was documented and graphed in Figures 10 and 11. The role of adjuvant chemotherapy was assessed in all of the reviewed cases and the reasoning for not receiving treatment was subsequently recorded. Patient refusal was the most common reason for non-treatment with adjuvant therapy (43.9%).

DISCUSSION

Similar studies reviewing the adherence to stage-specific treatment guidelines for patients with colon cancer based the definition of adherence on whether postoperative chemotherapy was actually recommended by the clinician, independent of whether it was actually received in stage II high risk and stage III patients. If a similar definition of adherence were used in this analysis, adherence rates to NCCN guidelines would significantly improve. As a result, there would have been 96.3% adherence in stage II high risk patients and 93.1% adherence in stage III patients using this definition as compared to 11.1% adherence in stage II high risk patients and 72.4% adherence in stage III patients in this study.

The NCCN currently estimates adherence to stage-specific management of colon cancer to be 66.0% in stage II low risk, 36.0% in stage II high risk, and 71.0% in stage III patients.[1] In comparison to the data collected in this analysis, adherence to NCCN guidelines was as follows: 84.2% of stage II low risk, 11.1% of stage II high risk, and 72.4% of stage III patients. The lower adherence to NCCN guidelines for stage II high-risk patients may be attributed to multiple factors including poor risk assessment in differentiating between the two stage II risk categories, and also related to physicians educating patients that though adjuvant chemotherapy is standard of care, there is only a small benefit of adjuvant chemotherapy in stage II colon cancer patients as it relates to disease free-survival and overall survival. The data supporting adjuvant chemotherapy in stage III colon cancer is strong and compelling.

Figure 10: Reasoning for No Treatment (Stage II High Risk)

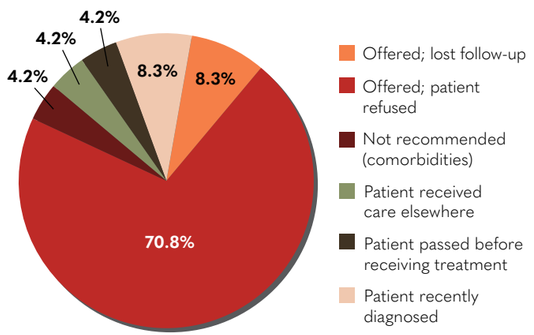


Figure 11: Reasoning for No Treatment (Stage III)

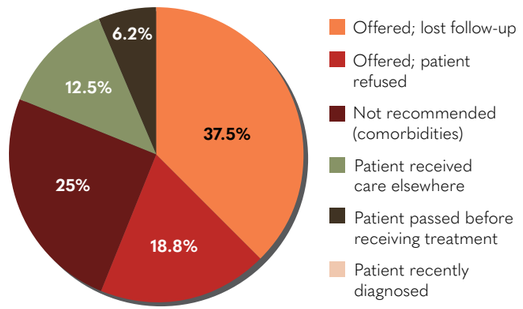
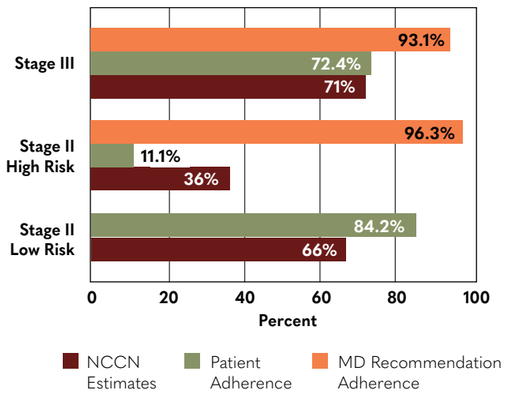


Figure 12: NCCN Guideline Adherence



To better distinguish between stage II low risk and stage II high risk patients – and thus distinguish between which patients should receive adjuvant chemotherapy treatment – a sample checklist for risk assessment should be utilized (Figure 13). Moreover, when this distinction is made, documentation should occur for the purpose of proper management and evaluation.

CONCLUSION

This compliance study demonstrates the Watson Clinic Cancer & Research Center's overall level of adherence to the National Comprehensive Cancer Network (NCCN guidelines for treating stage II and stage III non-metastatic colon cancer patients. Overall, the greatest level of adherence to NCCN management and treatment guidelines was demonstrated by the stage II low risk cohort.

In order to improve adherence to NCCN guidelines for management of stage II and III colon cancer patients, the following will be initiated into our current practice:

a) A pathology checklist for stage II risk assessment (low vs. high) to better distinguish which stage II colon cancer patients should receive adjuvant chemotherapy treatment (Figure 13).

b) A multi-disciplinary approach in which the responsibilities of each healthcare provider is delineated (Figure 14).

Additionally, more clinical studies evaluating the absolute benefit of chemotherapy in stage II high risk colon cancer patients are needed so as to have more compelling evidence for patients about the importance of adjuvant chemotherapy.

Future studies evaluating stage II and III non-metastatic colon cancer patients may be conducted at Watson Clinic to analyze the impact of adherence to NCCN guidelines and 5 year stage-specific survival outcome. Additionally, measuring the rate of adherence to NCCN guidelines for the evaluation and management of colon cancer patients following the implementation and use of the risk assessment tool and multidisciplinary approach should be performed.

Figure 13: Colon Cancer Risk Assessment Tool

Watson Clinic Cancer & Research Center
Pathology Stage II Colon Cancer Risk Assessment Tool

Patient Name _____ Patient MRN _____

Please check all that apply to this patient:

- ☐ Limited lymphadenectomy (fewer than 12 lymph nodes examined)
- ☐ T4 or localized perforation
- ☐ Bowel obstruction
- ☐ Lymphovascular invasion
- ☐ Perineural invasion
- ☐ Cancer grade 3 or 4
- ☐ Signet ring or mucinous cell histology
- ☐ Mismatch repair proficient (pMMR) or microsatellite instability positive (MSI low)
- ☐ Positive surgical margins
- ☐ Close surgical margins (< 2 cm)
- ☐ Unknown surgical margins

Figure 14: Multidisciplinary Approach for Colon Cancer Treatment and Management

Gastroenterology	• Colonoscopy (histology, size, polyp removal, lymph node involvement)
Surgical Oncology	• Preoperative labs (CMP, CBC, CEA) • Adequate surgical resection (≥12 lymph nodes removed) • Postoperative labs (CMP, CBC, CEA)
Pathology	• ≥12 lymph nodes evaluated during biopsy • Documentation of number of positive lymph nodes, tumor grade, depth of penetration, status of margins, and presence of lymphovascular invasion, perineural invasion, and/or tumor deposits
Medical Oncology	• Risk assessment tool • Chemotherapy treatment (within 12 weeks following surgery) • Imaging (abdominal/pelvic CT/MRI, chest CT/X-Ray)

REFERENCES

1. Boland GM, Chang GJ, Haynes AB, Chiang Y, Chagpar R, Xing Y, Hu C, Feig BW, You YN, Cormier JN. 2013. Association between Adherence to National Comprehensive Cancer Network Treatment Guidelines and Improved Survival in Patients with Colon Cancer. Cancer. 119(8):1593-1601.
2. Chagpar R, Xing Y, Chiang Y, Feig B, Chang G, You YN, Cormier JN. 2012. Adherence to Stage-Specific Treatment Guidelines for Patients with Colon Cancer. Journal of Clinical Oncology. 30(9):972-979.
3. Chang GJ, Rodriguez-Bigas MA, Skibber JM, Moyer VA. 2007. Lymph node evaluation and survival after curative resection of colon cancer: systemic review. Journal of the National Cancer Institute. 99(6):433.
4. Colon Cancer NCCN Evidence Blocks. National Comprehensive Cancer Network (NCCN). Version 2.2019. <https://www.nccn.org/professionals/physician_gls/pdf/colon_blocks.pdf>.
5. Dotan E, Cohen SJ. 2011. Challenges in the management of stage II colon cancer. Seminars in Oncology. 38(4):511-520.
6. "Genetic/Familial High-Risk Assessment: Colorectal." National Comprehensive Cancer Network (NCCN). Version 3.2017. <https://www2.tri-kobe.org/nccn/guideline/colorectal/english/genetics_colon.pdf>.
7. Gryfe R, Kim H, Hsieh ET, Aronson MD, Holowaty EJ, Bull SB, Redston M, Gallinger S. 2000. Tumor microsatellite instability and clinical outcome in young patients with colorectal cancer. The New England Journal of Medicine. 342(2):69-77.
8. Joseph Kannarkatt, Joe Joseph, Peter C. Kurniali, Anas Al-Janadi, and Borys Hrinczenko. Journal of Oncology Practice 2017 13:4, 233-241.
9. "Key Statistic for Colorectal Cancer" American Cancer Society. *American Cancer Society, Inc.* 2019. Web. 23 Apr 2019. <https://www.cancer.org/cancer/colon-rectal-cancer/about/key-statistics.html>.
10. Lima IS, Yasui Y, Scarfe A, Winget M. 2011. Association between receipt and timing of adjuvant chemotherapy and survival for patients with stage III colon cancer in Alberta, Canada. Cancer. 117(16):3833.
11. NCCN Guidelines for Patients: Colon Cancer. National Comprehensive Cancer Network (NCCN). 2018. <https://www.nccn.org/patients/guidelines/colon/index.html>.
12. NCCN Clinical Practice Guidelines in Oncology: Colon Cancer. National Comprehensive Cancer Network (NCCN). Version 2.2019. <https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf>.
13. Nelson H, Petrelli N, Carlin A, Couture J, Fleshman J, Guillem J, Miedema B, Ota D, Sargent D. 2001. Guidelines 2000 for Colon and Rectal Cancer Surgery. Journal of the National Cancer Institute. 93(8):583.
14. O'Connell MJ, Mailliard JA, Kahn MJ, Macdonald JS, Haller DG, Mayer RJ, Wieand HS. 1997. Controlled trial of fluorouracil and low-dose leucovorin given for 6 months as postoperative adjuvant therapy for colon cancer. Journal of Clinical Oncology. 15(1):246.
15. Ribic CM, Sargent DJ, Moore MJ, Thibodeau SN, French AJ, Goldberg RM, Hamilton SR, Laurent-Puig P, Gryfe R, Shepherd LE, Tu D, Redston M, Gallinger S. 2003. Tumor microsatellite-instability status as a predictor of benefit from fluorouracil-based adjuvant chemotherapy for colon cancer. The New England Journal of Medicine. 349(3):247-57/.
16. Rodriguez-Bigas MA, Lin EH, Crane CH. 2003. Surgical Management of Colorectal Cancer. Cancer Medicine. 6.
17. Saltz LB, Kemeny NE. 1996. Adjuvant chemotherapy of colorectal cancer. The Oncologist. 1(1-2):22-29.
18. Thiels CA, Naik ND, Bergquist JR, Spindler BA, Habermann EB, Kelley SR, Wolff BG, Mathis KL. 2016. Survival following synchronous colon cancer resection. Journal of Surgical Oncology. 114(1):80.
19. "What is Colorectal Cancer?" American Cancer Society. *American Cancer Society, Inc.* 2019. Web. 23 Apr 2019. <https://www.cancer.org/cancer/colon-rectal-cancer/about/what-is-colorectal-cancer.html>.

Retrospective Study of Side Effect Management Among Patients Diagnosed with Advanced Head and Neck, Melanoma, Lung, and Kidney Carcinoma Who Have Been Treated with Immune Checkpoint Inhibitors

EMILY ROZEN AND SHALINI MULAPARTHI, MD

INTRODUCTION

Immunotherapy is a cancer treatment that uses the body's own immune system to fight cancer. Dynamic interactions take place between the immune system and cancer cells whereby immune cells can detect genetic and cellular abnormalities present on cancer cells. Various mechanisms are in place to closely regulate the activation and function of immune system factors; however, malignant cells can also modulate immune cell activity thus evading recognition and destruction by the immune system. The immune system is capable of mobilizing immune effector cells in response to cancer cells. Immunotherapies harness the immune system to attack and destroy tumors by regulating molecules involved in immune cell activation. In doing so, immunotherapy seeks to activate or reactivate the antitumor immune response to overcome or circumvent the immune invasion or escape mechanisms employed by cancer cells and tumors.

Initial approaches to immunotherapy for cancer cells are focused on enhancing the immune system's antitumor response by targeting cytokines and other molecules responsible for regulating immune cell activity. Two examples are interleukin-2 and interferon alpha. Newer treatments include immune checkpoint inhibitors and CAR T cell therapies. Immune checkpoint inhibitors are a class of agents that target immune cell checkpoints such as programmed cell death–1 (examples are nivolumab and pembrolizumab), PD–1 ligand (examples include elotuzumab, avelumab, and durvalumab), and cytotoxic T-lymphocyte associated antigen 4 (ipilimumab). Indications for immune checkpoint inhibitors have expanded dramatically and now include patients with lung, head and neck, bladder, kidney, gastric, ovarian, and liver cancers as well as melanoma, Hodgkin's lymphoma, Merkel cell carcinoma, and tumor deficient in DNA mismatch repair mechanisms. Immunotherapy which was initially indicated for advanced disease has now moved into early treatment settings.

This study is a retrospective study of side effect management among patients diagnosed with advanced head and neck cancers, melanoma, lung,

and kidney cancers who were treated with immune checkpoint inhibitors at Watson Clinic Cancer & Research Center. The study was done to determine if patients are on an appropriate treatment plan using National Comprehensive Cancer Network (NCCN) guidelines as a benchmark.

METHODOLOGY

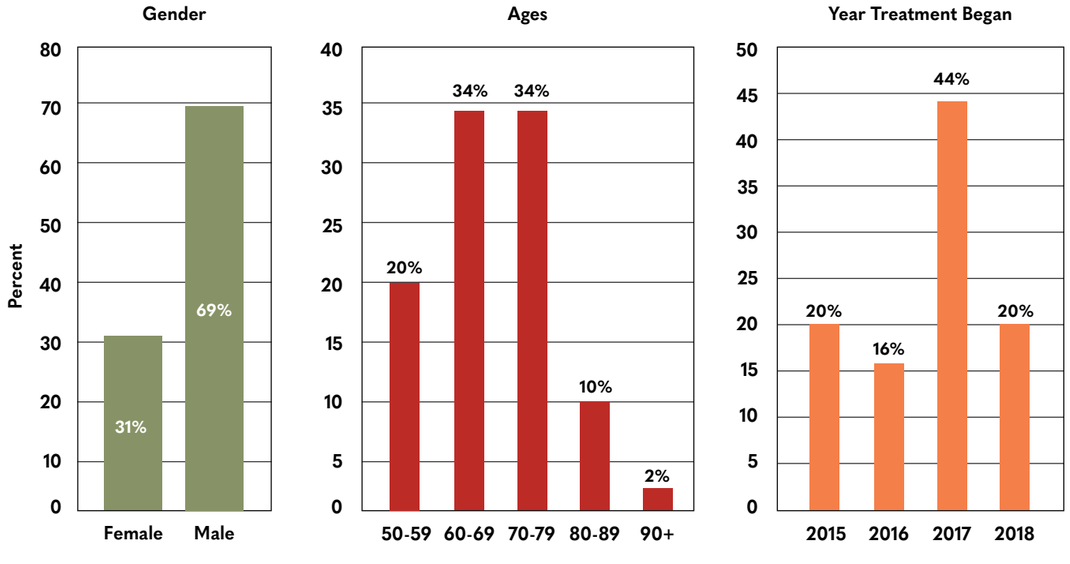
After receiving IRB approval, a list of patients diagnosed with advanced head and neck melanoma, lung, and kidney cancers who were treated with immunotherapy during the timeframe of January 1, 2015 to June 30, 2018 was compiled from the Watson Clinic Cancer & Research Center Cancer Registry. A total of 79 patient charts were reviewed with 45 being abstracted and 34 being excluded for various reasons. HIPAA research confidentially requirements were followed during data extraction in order to protect patient information. From these 45 patients' charts, 50 different administrations of immunotherapy were abstracted.

According to the NCCN guidelines, the primary facets of immunotherapy associated toxicity management include recognition and grading of toxicity immunosuppression and individualized modification to immunotherapy administration. Early recognition of symptoms and prompt intervention are key goals for the management of immunotherapy related toxicity. Significant toxicities often led to holding immunotherapy, and permanent discontinuation of the class of agent associated with a toxicity in the case of certain severe toxicities

DEMOGRAPHICS

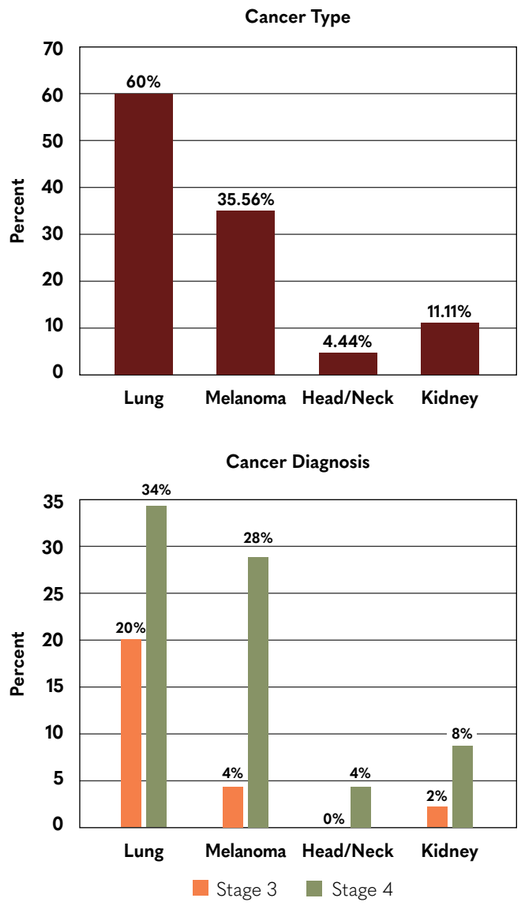
Patient demographics (Figure 1) included 31% female and 69% male. Ages were between 50 and 90 years, with the majority of the patients in the range of 60-79 years (68% patients). In 2015, 20% of the patients received immunotherapy, in 2016 16% of them received immunotherapy, in 2017 44% received immunotherapy, and from January-June 2018 20% received immunotherapy (study data collected through June 2018).

Figure 1:



Patients with lung cancer dominated immunotherapy treatment, melanoma contributed to 35% of the patients, kidney cancer 11%, and head and neck cancer 4%. Staging data was also abstracted, with lung cancer stage III occurring in 20% of the patients receiving immunotherapy and 34% of the patients with stage IV receiving immunotherapy. Stage III melanoma was present in 4% of patients receiving immunotherapy, and 28% had stage IV melanoma. All head and neck cancers were advanced (stage IV). Stage III kidney cancer accounted for 2% of patients, and stage IV disease was present in 8% of patients (Figure 2).

Figure 2:



TREATMENT

Pembrolizumab was received by 38% of the patients, nivolumab was received by 42%, durvalumab was received by 4%, ipilimumab was received by 12%, and a combination nivolumab and ipilimumab was received by 4% of the patients (Figure 3). Immunotherapy and chemotherapy combination was used in 20% of the patients while immunotherapy alone was given in 80% of the patients (Figure 4).

Figure 3:

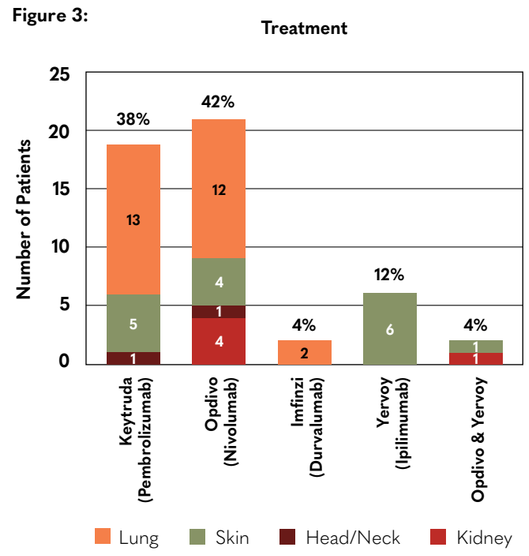
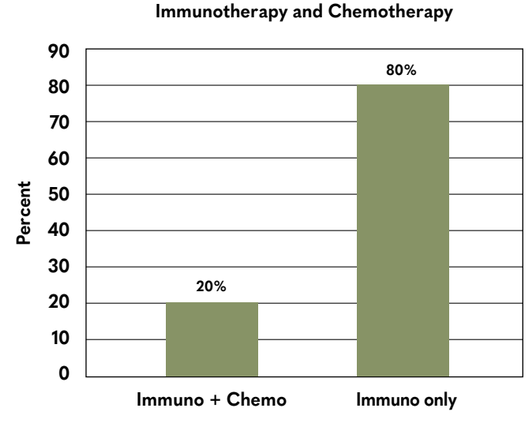


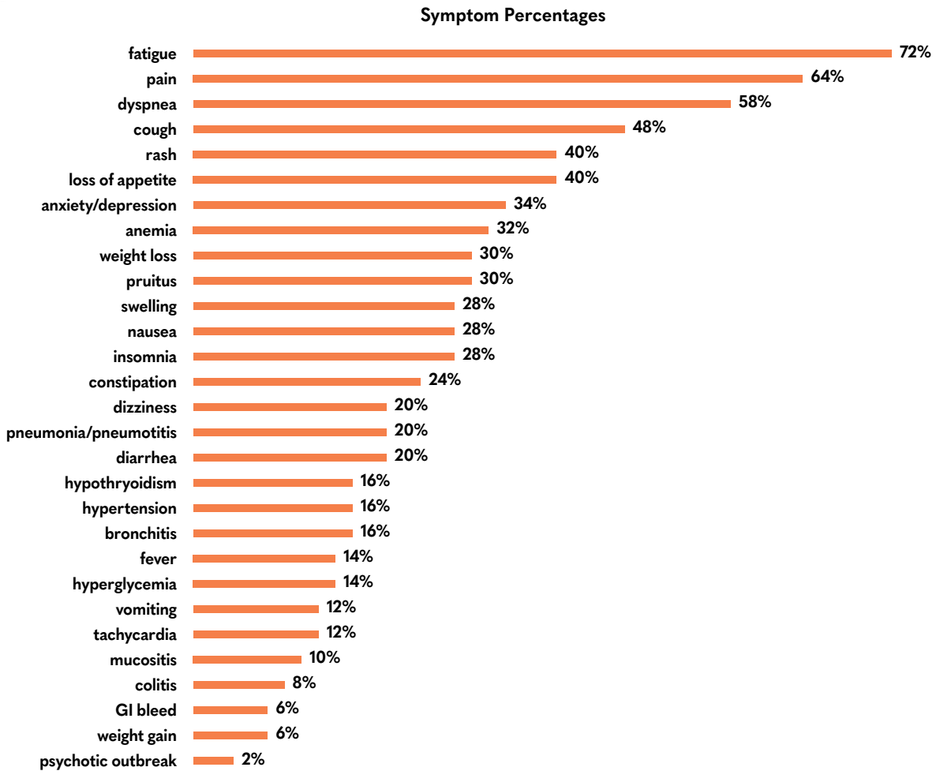
Figure 4:



SYMPTOMS

Fatigue was a prevalent symptom in patients receiving immunotherapy treatment representing 72% of patients treated, followed by pain at 64%, dyspnea at 58%, and cough at 48%. Other noted symptoms are represented in Figure 5.

Figure 5:



MANAGEMENT OF IMMUNE THERAPY RELATED SIDE EFFECTS/TOXICITY

General Principles of Immune Suppression

Corticosteroids are the mainstays of treatment for most high-grade adverse events. Importantly, short-term use of corticosteroids to treat immunotherapy related side effects has not been shown to reduce antitumor efficacy. Appropriate duration and careful taper of corticosteroid therapy is important to prevent the recurrence of immune related side effects. Severe or corticosteroid refractory adverse events may require administration of additional immunosuppressive agents for patients with severe adverse events not responsive to steroids within 48 to 72 hours. Initiation of an additional immunosuppressant agent may be warranted in consultation with the relevant medical specialist. Close monitoring and follow-up should be performed to assess for response for two corticosteroids

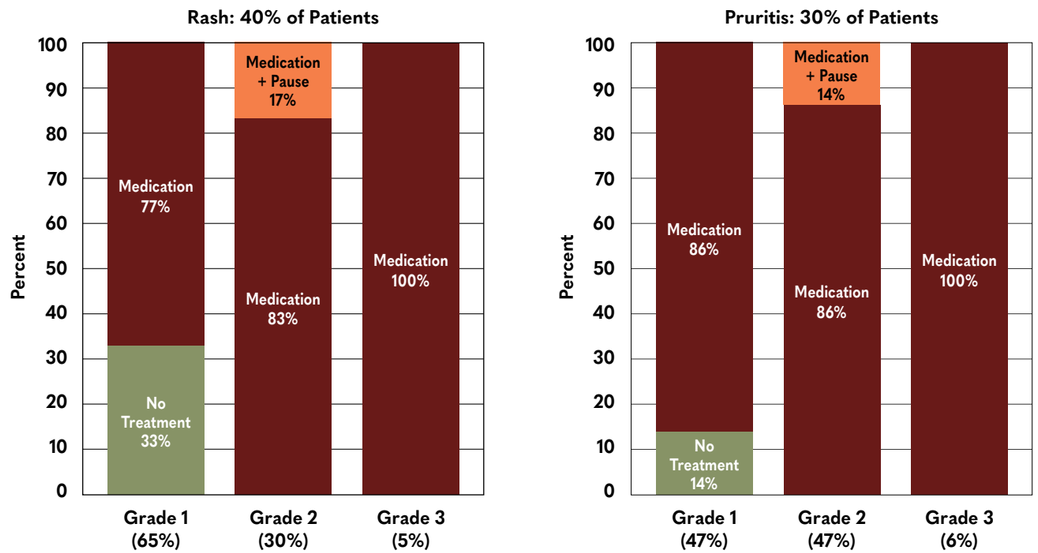
and other immunosuppressants in the setting of immunotherapy related toxicity. Immunomodulators, including immunosuppressive agents, intravenous immunoglobulin, and in severe cases plasmapheresis, have been used to suppress a wide area of autoimmune and chronic inflammatory conditions. Additional supportive care measures are needed for patients receiving an immunosuppressive regimen.

Dermatologic Toxicity

Forty percent of the patients developed a rash and 30% of the patients had pruritus (Figure 6). Of patients with grade one rash, 77% received medication. Medication was received by all patients with grade two rash, and 17% of these patients had their treatment put on hold; however, of patients with grade three rash, 100% of them received medication none of them had treatment put on hold.

Grade one pruritis was seen in 47% of the patient with pruritis, of which 86% received medication. Grade two pruritis was seen in 47% of the patients, with all receiving medication, and 14% had treatment put on hold. Five percent developed grade three pruritis requiring medication. Treatment given for these patients included topical and oral steroids and antihistamines none of them received a dermatologic evaluation.

Figure 6:



Gastrointestinal Toxicity

Toxicities including mucositis, diarrhea, colitis, constipation and elevated liver function tests were noted. Ten percent of the patients developed mucositis. Grade two mucositis was seen in 40% of these patients and grade three mucositis was seen in 60% of these patients. Treatments including Magic mouthwash and holding treatment for severe mucositis were documented (Figure 7).

Diarrhea was seen in 20% of the patients. Eighty percent of these patients had grade one toxicity with 75% of them requiring medication, 10% had grade two and 10% had grade three, with 100% of both grades requiring medication and a hold of treatment (Figure 8).

Colitis was seen in 8% of the patients. Grade one was seen in 25% of these patients and did not require treatment. The 25% of patients with grade two and 25% with grade three colitis received medication. All patients with grade four (25%) colitis had treatment held and required medication.

Constipation was seen in 24% of the patients, with grade one representing 75% and grade two representing 25%. Treatment was needed with medications including increasing fiber in the diet.

Figure 7:

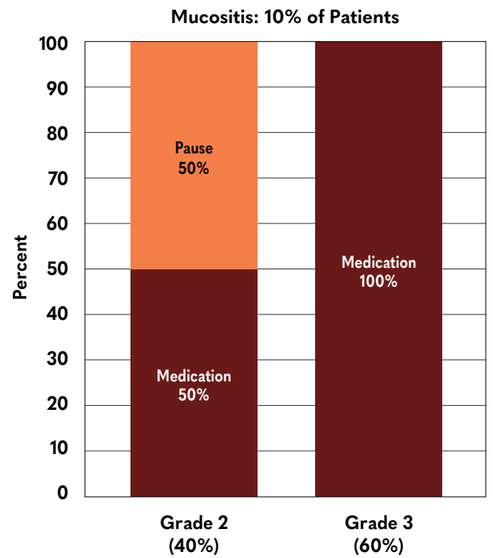
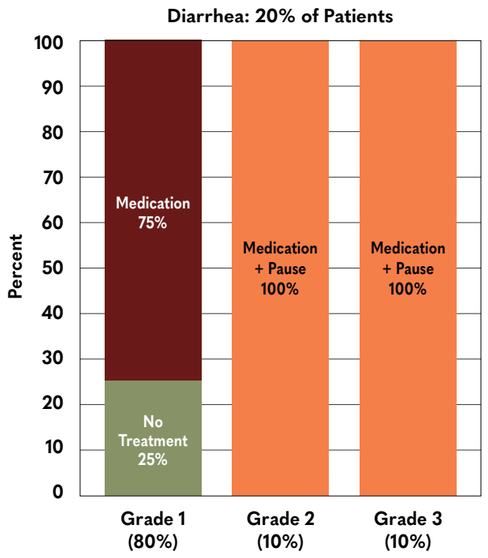
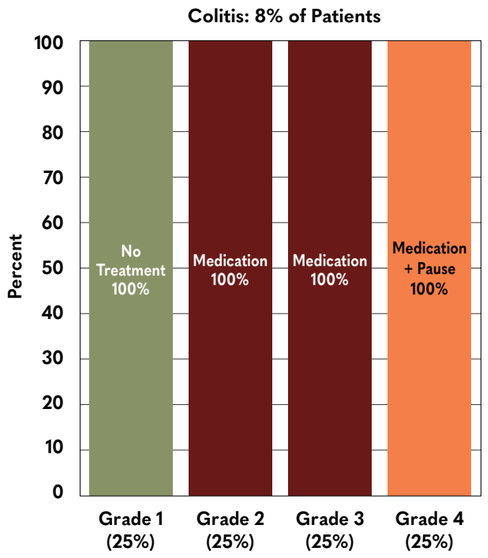


Figure 8:





Endocrine Toxicity

Elevated liver enzymes were seen in 18% of the patients, with 56% having grade one, 22% with grade two, and 22% with grade three. Close monitoring for all patients was documented. Endocrine toxicity with hypothyroidism grade two toxicity was seen in 16% of the patients, all requiring medication and close monitoring of TSH levels (Figure 9).

Hypophysitis was mentioned in differential diagnosis without clear diagnosis; however, patients did have symptoms of chronic fatigue and weight loss. Primary adrenal insufficiency was not documented. Hypoglycemia was seen in 2% of the population.

Pulmonary Toxicity

Pulmonary toxicity including pneumonitis, dyspnea, and cough was documented (Figures 10-11). Dyspnea was seen in 58% of the patients (grade one toxicity in 41%, grade two toxicity in 20%, grade three toxicity in 31%, and grade four toxicity in 9%). Treatment included inhalers, thoracentesis and oxygen evaluation.

Cough was documented in 48% of the patients, 29% with grade one, 71% with grade two. Treatment included cough suppressants.

High-grade pneumonitis was documented in 4% of the patients. These patients required medications

Figure 9:

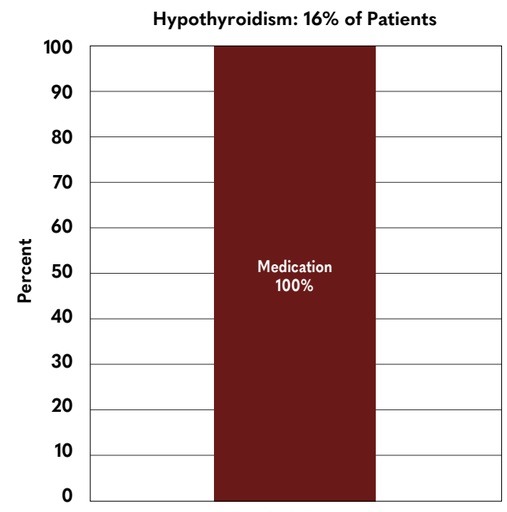


Figure 10:

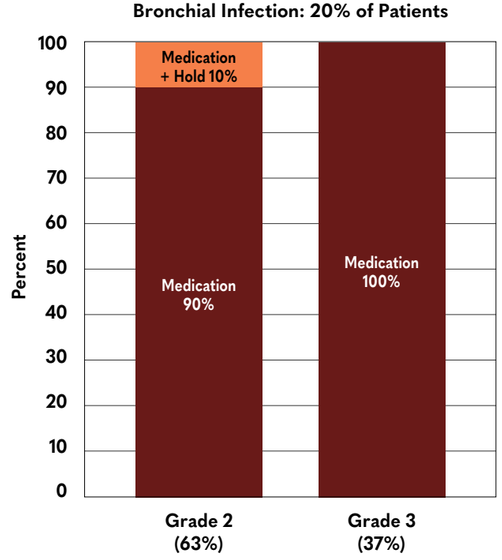


Figure 11:

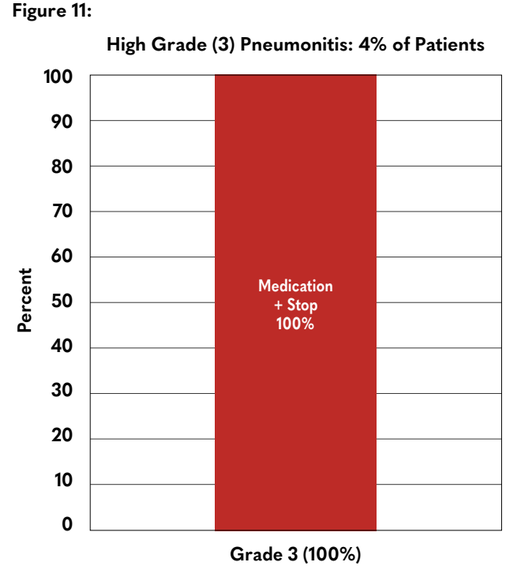
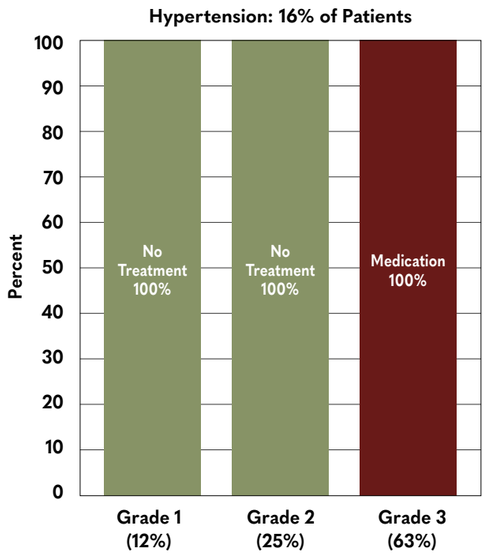


Figure 12:



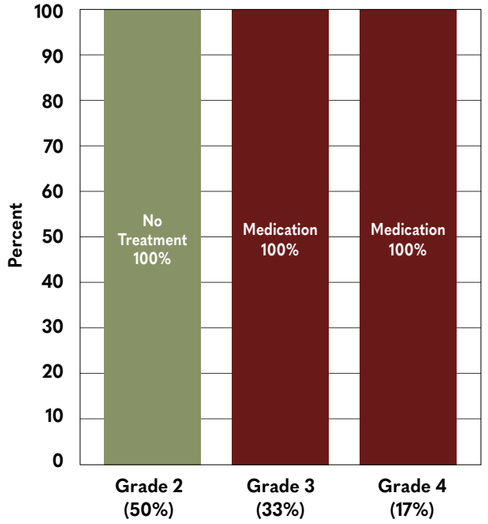
including steroids, inhalers and hospital admission oxygen treatment.

Cardiac Toxicity

Hypertension was seen in 16% of the patients, with grade one toxicity in 12%, grade two toxicity in 25%, and grade three toxicity in 63% of the patients. Grade three toxicity required beta-blockers diuretics. Tachycardia was seen in 12% of the patients, with grade three and four requiring beta-blockers (Figure 12).

Dizziness (Figure 13) was seen in 20% of the patients, with grade two requiring medications including fludrocortisone, IV fluids, and discontinuation of blood pressure medications.

Figure 13:



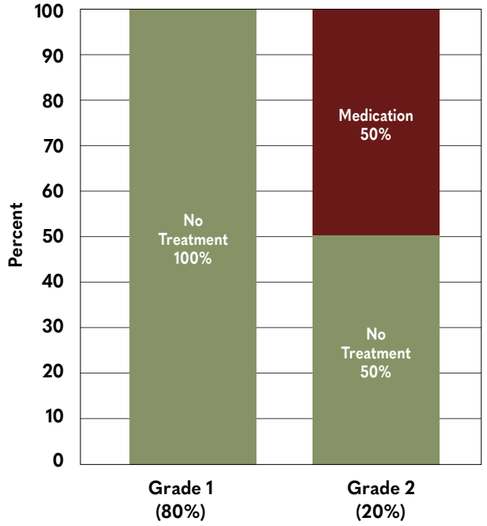
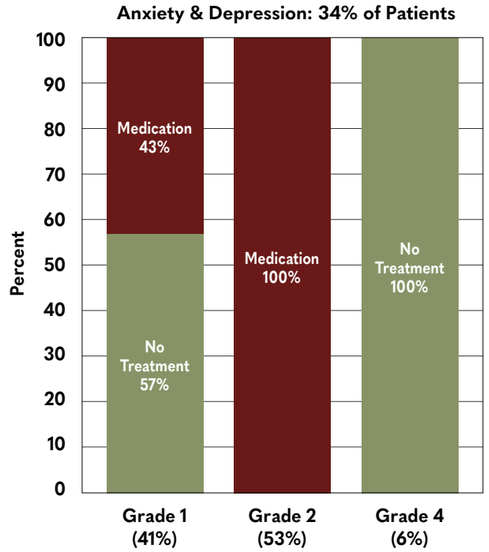


Figure 14:



Neurological toxicity

Anxiety and depression was seen in 34% of the patients (Figure 14). Forty-three percent of grade one patients required medication. Patients with grade two toxicity required medications including Lexapro and Zoloft, and one patient had to be hospitalized for psychotic behavior.

Insomnia was reported in 28% of the patients with 100% of patients with grade two or three insomnia requiring medications (Figure 15).

Pain symptoms were seen in 64% of the patients, with a majority of the patients requiring pain medication, and some requiring a hold on treatment (Figure 16).

72% of the patients required hospitalization for immunotherapy related side effects.

Figure 15:

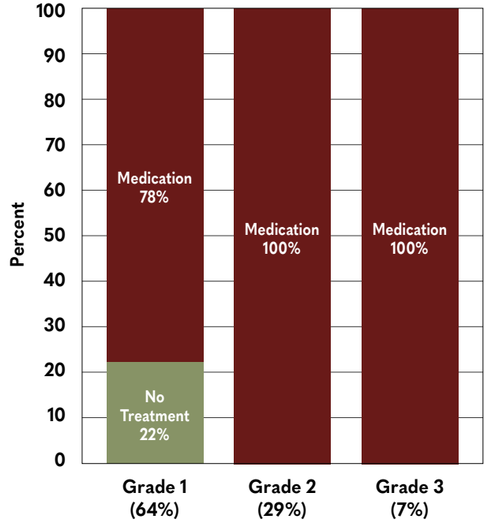
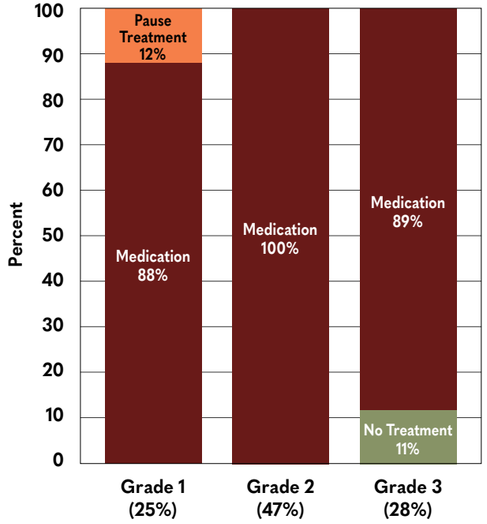


Figure 16:



CONCLUSION

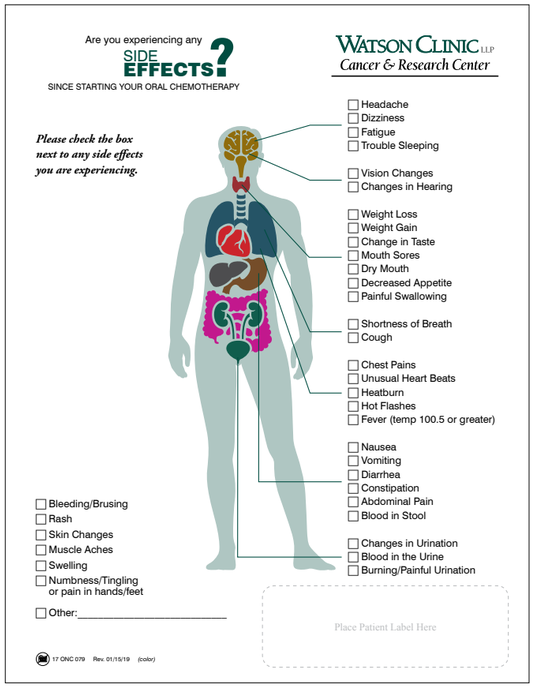
Documentation problems have led to a decrease in properly addressing side effects of patients treated with immunotherapy. When addressed, side effects are well managed; however, side effects are not always addressed or documented. Our doctors were treating patients based on their symptomatology, as we did not have guidelines for symptom documentation; however, treatment was not compromised, only documentation was a problem. Tests such as TSH are not always ordered when they should be. It is difficult to determine if side effects are from immunotherapy alone or combination of immunotherapy plus chemotherapy; however, we should still treat symptoms according to guidelines.

PLAN FOR IMPROVEMENT

We are implementing a Patient Side Effect Sheet (Figure 17) for every patient with immunotherapy, and are working with Watson Clinic Informatics to build a symptom grading system in EPIC.

We thank the Watson Clinic Cancer Registry for providing information from the registry database.

Figure 17:



Resources & Information on Cancer

A Place For Her
727-447-1146 • www.aplaceforher.com

American Cancer Society (ACS)
800-227-2345 • www.cancer.org

American College of Surgeons (ACoS)
800-621-4111 • www.facs.org

American Institute for Cancer Research (AICR)
800-843-8114 • www.aicr.org

American Lung Association
www.lungassociation.org

Breast Cancer Foundation of Central Florida
417-862-3838 • www.bcfcf.org

CancerCare
800-813-HOPE • www.cancercare.org

Centers for Disease Control and Prevention (CDC)
www.cdc.gov

Central Florida Health Care Center
866-234-8534 • www.cfhconline.org

Chronic Disease Fund
877-968-7233 • www.cdfund.org

Citrus Connection Handy Bus
www.ridecitrus.com

Comfort Keepers
866-225-0320 • comfortkeepers.com

Commission on Cancer (CoC)
312-202-5009 • www.facs.org/cancer

Cornerstone Hospice
866-742-6655 • web.cshospice.org

Department of Children and Families
407-317-7000 • www.myflfamilies.com

Florida Cancer Data System (FCDS)
305-243-4600 • www.fcds.med.miami.edu

Florida Department of Health (FDH)
www.doh.state.fl.us

Good Shepherd Hospice
800-544-3280 • www.chaptershealth.org

Healthwell Foundation
800-675-8416 • www.healthwellfoundation.org

Lakeland Volunteers in Medicine
863-688-5846 • www.lvim.net

Leukemia & Lymphoma Society
800-955-4572 • www.leukemia-lymphoma.org

Lighthouse Ministries
863-687-4076 • www.lighthousemin.org

National Cancer Institute (NCI)
800-4CANCER • www.cancer.gov

Nurses Helping Hands Assisted Living
www.nurseshelpinghandsalf.com

Patient Access Network
866-316-7263 • www.panfoundation.org

Patient Advocate Foundation
800-532-5274• www.patientadvocate.org

Patient Services, Inc.
800-366-7741 • www.patientservicesinc.org

Polk County Elderly Services
863-534-5320 • www.polk-county.net

Polk County Transport
www.polk-county.net

Social Security Administration
www.ssa.gov

Susan G. Komen
800-468-9273 • www.komen.org

Talbot House
863-687-8475 • www.talbothouse.org

United Way
2-1-1 or 863-648-1515 • www.uwcf.org

VITAS Hospice
863-583-7100 • www.vitas.com

Volunteers In Service to the Elderly (VISTE)
863-284-0828 • www.viste.org

We Care of Polk County
863-662-4227 • www.wecarecentralflorida.org

WATSON CLINIC LLP
Cancer & Research Center

1730 Lakeland Hills Boulevard • Lakeland, FL 33805 • 863-603-4770 • www.WatsonClinic.com/CancerCenter