**Needs Assessment**: Optimizing Treatment in Locally-Advanced Rectal Cancer

**Target Audience**: Oncologists, General and Colorectal Surgeons, Radiation Oncologists, NPs, other clinicians involved in treatment

**Possible Grant Supporters**: *Sanofi*-Eloxatin, *Genentech-* Xeloda, National Cancer Institute

**Date**: April 26, 2018

**Proposed Activity**: Lecture Series

**Activity #1:** Locally-Advanced Rectal Cancer: Screening and Current Management

**Introduction**

Colorectal cancer is the third most commonly diagnosed cancer in the United States. Rectal cancer comprises 28% of the total cases of colorectal cancer, with approximately 40,000 new yearly cases predicted. The incidence of colorectal cancer is decreasing in the population over 50 due to increasing screening and earlier treatment. It is increasing in the population below 50 at a rate of 3.9% per year. The increase in younger patients is attributed to the obesity epidemic and sedentary lifestyle. Progress can be achieved in this patient population by addressing the importance of an active lifestyle, encouraging weight loss, continuing to increase screening in average risk patients at age 50, and earlier screening in the higher risk population. (Siegel)

Rectal cancer is staged with assessment of three factors: tumor size and location, evidence of lymph node involvement, and evidence of distant disease. Pretreatment diagnostic staging is critical to determine the individual treatment plans for patients. After colonoscopy and biopsy is performed, a typical workup will include a CT scan, a CEA level, and an endorectal ultrasound. MRI and CT-PET scan are also commonly employed. (Wu) Staging guidelines have been established by the American Joint Committee on Cancer (AJCC) which are the most accurate guidelines to follow and are based on the Tumor, Node, Metastasis (TNM) system. (Monson)

 The standard approach to rectal cancer is multimodal treatment with preoperative radiation, surgery, then systemic chemotherapy when indicated. Studies evaluating chemotherapy have been difficult to complete due to poor compliance and inconsistent survival rates. Recent trials with neoadjuvant radiation and chemotherapy have demonstrated an improvement in survival and organ preservation. (Ludmir) Clinical guidelines for the treatment of rectal cancer are published by such organizations as the National Comprehensive Cancer Network(NCCN) and the American Society of Colon and Rectal Surgeons. Due to the developments of treatment of rectal cancer in the past 10 to 15 years, education in these developments is needed so that treatment plans can be developed for patients in light of these advances. ( Monson)

**Goal** This activity will increase clinician knowledge and awareness with respect to the current definition, staging and treatment of locally-advanced rectal cancer.

**Methodology**

The following sources of information were used to develop clinical practice gaps and educational needs:

1. Medical Literature Review

2. Clinical Practice Guidelines

**Clinical Practice Gap #1 Clinicians may not familiar with best practice for initial evaluation of locally-advanced rectal cancer to develop counseling and treatment options.**

 Complete pretreatment evaluation of patients with newly-diagnosed rectal cancer is integral to determine treatment and to facilitate sphincter preservation. (Weiser) Adding chemotherapy, pre- or post surgery, has been demonstrated to improve local control of rectal cancer and aid in sphincter preservation in patients with locally-advanced disease. (Bosset) Poor compliance with chemotherapy has been demonstrated to adversely affect survival regardless of stage. In a recent study, 68% of patients did not receive adjuvant chemotherapy who were qualified to receive it. (Xu) Chemotherapy has also been demonstrated in to improve survival in the elderly, regardless whether it was preoperative or postoperative. (Bergquist)

 NCCN guidelines for evaluation recommend full colonoscopy when possible, preoperative CEA level, and evaluation for local and distant metastatic disease. This metastatic workup would include either endorectal ultrasound and CT scan or MRI. (NCCN) These tests allow for accurate preoperative staging of patients. Endorectal ultrasound and CT or MRI combined with/without CT-PET has shown promise to stage rectal lesions after preoperative neoadjuvant therapy. However, CT-PET is not currently indicated in pretreatment assessment. (Muthusamy)

 While many methods are employed in the staging of rectal cancer, there is some debate between best appropriate testing. Endorectal ultrasound is useful to determine local extent of disease prior to treatment, but is not accurate in post radiation assessment due to surrounding tissue inflammation. (Heo) CT the most common radiologic study used to evaluate distant metastatic lesions, but its utility is limited. (Heo) High-resolution MRI has demonstrated improvement over other previously employed methods. MRI enables accurate staging of both early and advanced rectal cancer, accurate response assessment, the delineation of recurrent disease and planning surgical treatment in a safe and effective manner. MRI is also accurate in stratifying treatment response into low and high tumor responders which helps to guide future therapy.( Balyasnikova)(Hunter)

 Accurate pretreatment staging is necessary due to developments in surgical approach and adjuvant therapy. Surgical options for treatment include abdominoperineal resection with colostomy placement, resection with anastomosis, and local excision with possible partial excision of the sphincter muscle. Total mesorectal excision (TME) is excision of the rectum and meticulous excision of the surrounding lymphatic drainage of the rectum and local fascial planes. TME alone improves local recurrence from 15-45% to 8%. Surgery with total mesorectal excision and preoperative radiotherapy resulted in a local recurrence rate of 2.4% at 5 years. (Kapitijn) Preoperative staging involves principles of determining surgical therapy and risk stratification in determining adjuvant therapy.(Evans)

**Educational Need #1** *Clinicians need education in best practice for treatment of locally-advanced rectal cancer for counseling and treatment options.*

**Clinical Practice Gap#2 Clinicians may be unfamiliar with new treatment options which exist for delivery and regimen of chemotherapy with locally-advanced rectal cancer.**

Preoperative chemoradiation and total mesorectal excision have decreased local recurrence rates in rectal cancer from 32-35% to 4-9%.(Kapitijn) The central problem to be addressed is distant recurrence. (Boland) Preoperative chemoradiation and TME is currently the accepted approach for treatment of locally-advanced rectal cancer, but there have been recent changes to the regimen of adjuvant chemotherapy. Meta-analysis of 21 randomized controlled trials advocates for this practice in rectal cancer. It established a 25% reduction in risk of recurrence using adjuvant 5-FU based regimens in rectal cancer patients.(Peterson)

In 2014, EORTTC 22921 reported no survival benefit to a regimen of 5-FU and leucovorin. (Bosset) However, since this regimen lacked oxaliplatin and the compliance rates were so poor, this data was regarded with skepticism. (Boland) Oxaliplatin is the only drug which conclusively improves outcomes in the adjuvant setting for early stage colorectal cancer. However, toxicity and poor compliance with postoperative administration continue to be an limiting factor. (deGarmont)

 In locally-advanced rectal cancer, neoadjuvant treatment has improved clinical results. The combination of multiple modalities, to improve compliance and reduce toxicity, demonstrates a measured benefit. Selection of the optimal patient population for each regimen through appropriate staging workup is key. Currently, the PROSPECT trial (Preoperative Radiation or Selective Preoperative Radiation and Evaluation before Chemotherapy and TME) is challenging the current treat paradigm. It is an opportunity to reduce pelvic irradiation for those who may not benefit from it. It is also an effort to focus systemic therapy earlier in the treatment regimen to reduce distant recurrence. (Weiser)

 Total Neoadjuvant Therapy(TNT) is a newly accepted regimen currently in phase II/III trials. It is comprised of 6 months of induction chemotherapy, followed by chemoradiation therapy, and then followed by surgery. (Cerek) In some patients who achieve a complete clinical response, the decision has been made to forego surgery. This decision is especially considered in patients who would have required an abdominoperineal resection or a very distal low anterior resection. One small prospective study which employed TNT and watchful waiting observed a higher rate of local recurrence after nonsurgical treatment, but 59% of patients were able to avoid surgery. (Habr-GAMa)

**Educational Need #2** *Clinicians need education of the different regimens of chemotherapy for locally-advance rectal cancer so they may choose the regimen which holds the most benefit for their patient.*

**Conclusion**

 Patients with locally-advanced rectal cancer need an accurate and complete pretreatment evaluation. This will stratify them into accurate risk stratification groups which will determine their best treatment strategy. Established clinical guidelines outline evaluation and treatment. Despite the presence of these guidelines, many patients do not complete the recommended course of therapy. Physicians in the practice of treating these patients state and observed hesitancy on the part of physicians in the community to adapt to the newly accepted standards of practice.(Hong) To address this gap in treatment, this activity will:

 • Review the workup of of a patient diagnosed with rectal cancer with an emphasis on accurate pretreatment and preoperative staging

 • Discuss the different surgical options available for patients depending on the location of the rectal tumor and tumor bulk

 • Delineate the different protocols for treatment with adjuvant and neoadjuvant therapy

 • Present the data which outline and support the watchful waiting approach to surgery in the presence of a complete clinical response to neoadjuvant therapy

***Educational Planning Table***

**Clinical Practice Gap #1 Clinicians may not familiar with best practice for initial evaluation of locally-advanced rectal cancer to develop counseling and treatment options.**

**Educational Need #1** *Clinicians need education in best practice for treatment of locally-advanced rectal cancer for counseling and treatment options.*

**Learning Objectives**

**Outcome Measures**

 • Define staging system for rectal cancer

 and pretreatment workup to establish this

 stage

 • Delineate treatment options for rectal

 cancer based on stage and tumor location

Level 3(Knowledge): Multiple-choice items designed to assess knowledge of staging of rectal cancer and pretreatment workup

Level 4(Competency):Case-based multiple-choice items designed to assess participants’ ability to apply guidelines for appropriate workup and staging of rectal cancer.

**Clinical Practice Gap#2 Clinicians may be unfamiliar with new treatment options which exist for delivery and regimen of chemotherapy with locally-advanced rectal cancer.**

**Educational Need #2** *Clinicians need education of the different regimens of chemotherapy for locally-advance rectal cancer so they may choose the regimen which holds the most benefit for their patient.*

**Learning Objectives**

**Outcome Measures**

 • Define surgical options for treatment

 • Discuss adjuvant and neoadjuvant therapies including chemotherapeutic agents.

Level 3 (knowledge): Multiple-choice items designed to assess changes related to knowledge of emerging clinical treatment data.

Level 4 (competence): Case-based multiple-choice items designed to assess participants’ ability to select appropriate treatment options for patients with locally-advanced rectal cancer.

**Activity #1** Locally-Advanced Rectal Cancer: Staging, Workup, and Treatment

**Learning Objectives**

After taking part in this activity, participants should be able to:

 1. Evaluate patients with newly-diagnosed rectal cancer and accurately stage their disease

 2. Define treatment options for their disease based on staging and counsel them appropriately

 3. Execute therapy based on their clinical role and newly-defined treatment guidelines

**Proposed Agenda**

Introduction

 • Definition of the epidemiology of rectal cancer

 • Background of historical treatment strategies and developments

Staging and Counseling Guidelines

 • Definition of TMN Staging system

 • Current Data for Radiologic Evaluation in the Staging Process

 • NCCN Staging and Treatment Guidelines

 • Treatment Recommendations from the American Society of Colon and Rectal Surgeons

Management of Locally Advanced Rectal Cancer

 • Surgical options for treatment

 • Total Mesorectal Excision Description and Methodology

 • Neoadjuvant versus Adjuvant Chemotherapy treatment Strategies

 1. 5-Fluorouracil

 2. Leucovorin

 3. Oxaliplatin

 4. Xeloda

Discussion of the debate concerning Watchful Waiting with complete clinical response and clinical trials

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