

Updates in Local Therapy for Rectal Cancer In Young-onset Patients:

Radiation & Surgery

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M.D. Anderson Cancer Center**

Outline

Review rationale: The 10,000 Ft. View

**New updates: Radiation
To Escalate or De-Escalate?**

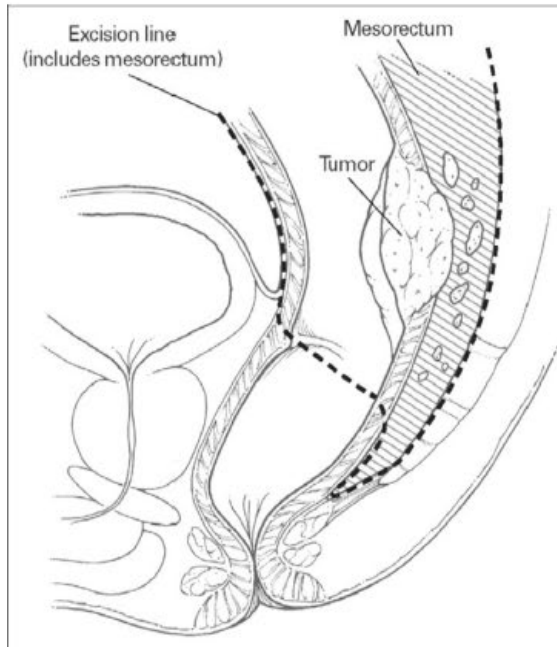
**New updates: Surgery
Omitting surgery / Organ preservation?**

Introduction

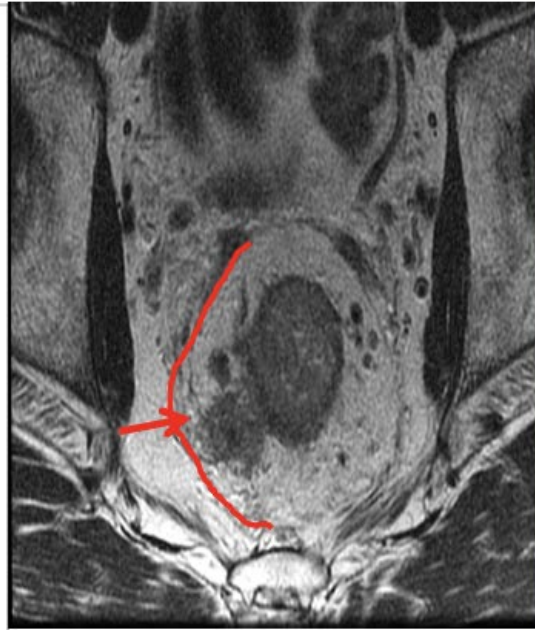
The 10,000 Ft. View



Surgery = Backbone For Local Control



**Total Mesorectal
Excision**



**Circumferential
Resection Margin**



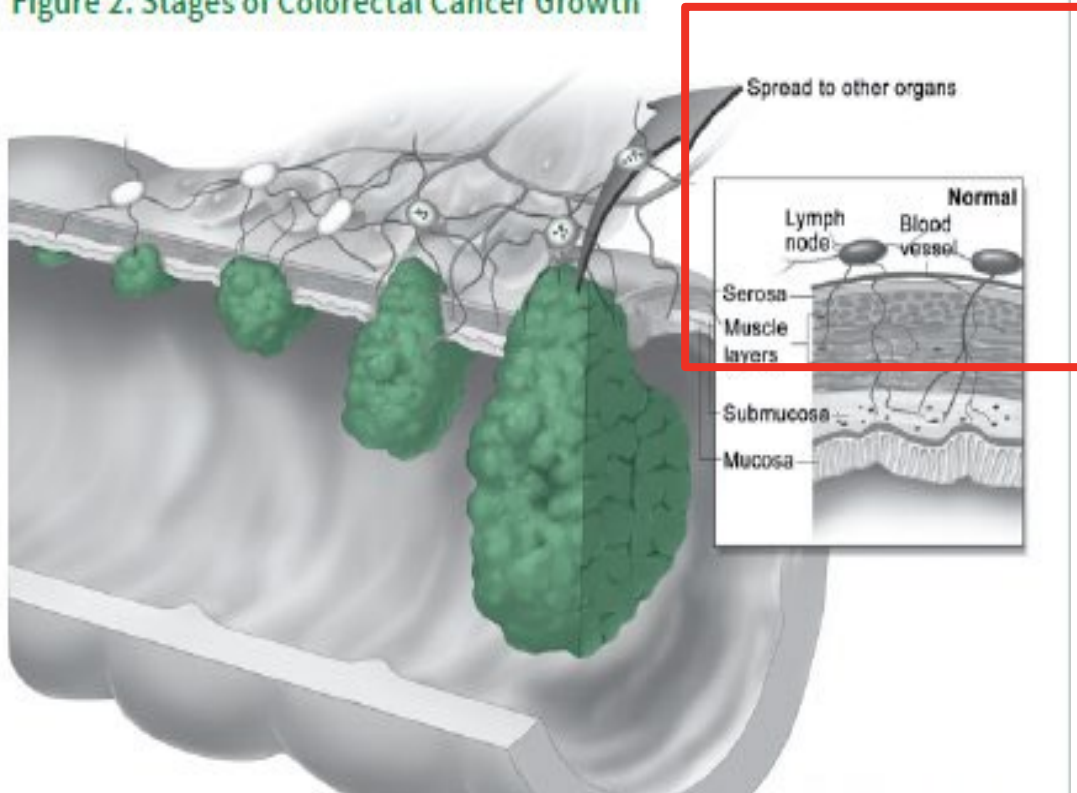
**Regional
Lymphadenectomy**

Principles of Optimal local control

- Extent and integrity of primary tumor resection : **Proximal/Distal margins**
- En bloc resection of involved adjacent viscera: **Radial margins**
- Adequacy of lymph node resection: **Vascular dissection, nodal harvest**

Surgery *PLUS* = Building On Backbone For Local Control

Figure 2. Stages of Colorectal Cancer Growth



**Locally advanced
rectal cancer:**

Need Surgery *Plus* !

- Radiation
- Chemotherapy

Surgery = Changes Anatomy and therefore also Physiology

Key Factors Impacting Physiologic Sequelae

1. Which **part** of the colorectum was resected
2. What was the **extent (length)** of resection
3. Was there a **complication**
4. Was **radiation** used
5. Is there an **ostomy**
6. What was the **baseline function** (# stools/day, sphincter function)
7. Any **underlying medical condition** (inflammatory bowel disease, connective tissue disorder, etc)

Functional Sequelae of Pelvic Surgery

Low Anterior Resection Syndrome

Symptoms



Variable, unpredictable bowel function



Emptying difficulties



Altered stool consistency



Increased stool volume



Urgency

Consequences



Toilet dependence



Impact on:
Mental and emotional wellbeing



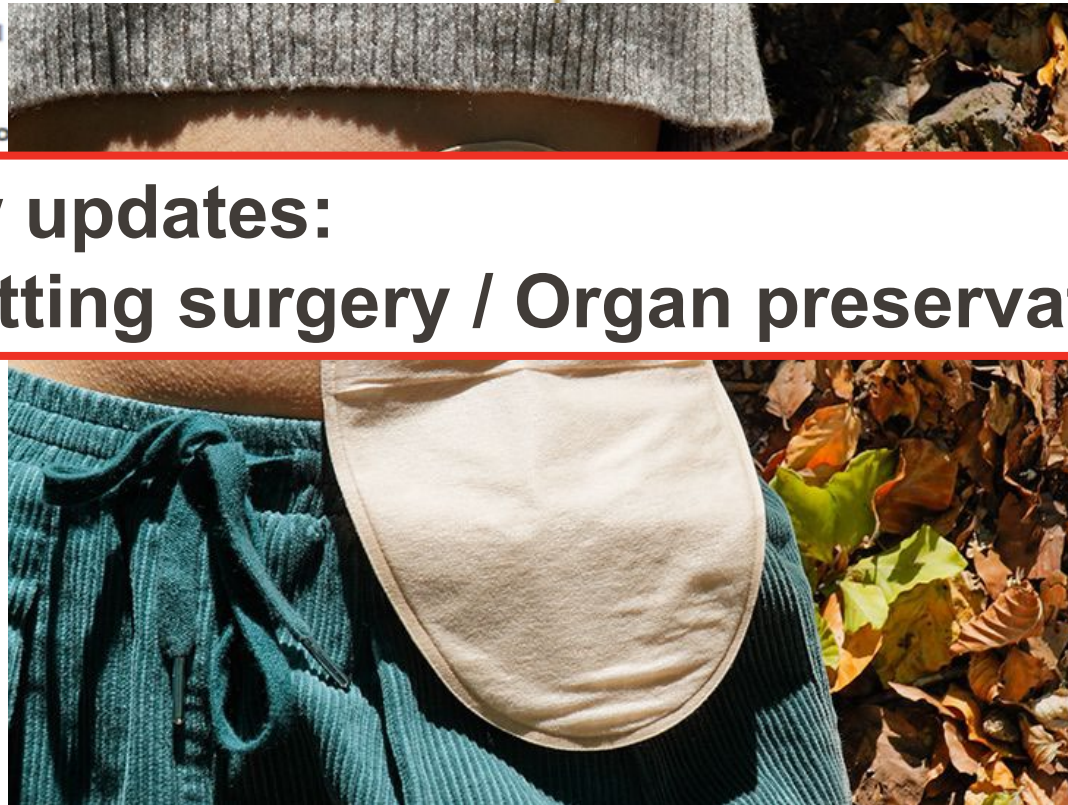
Social and daily activities



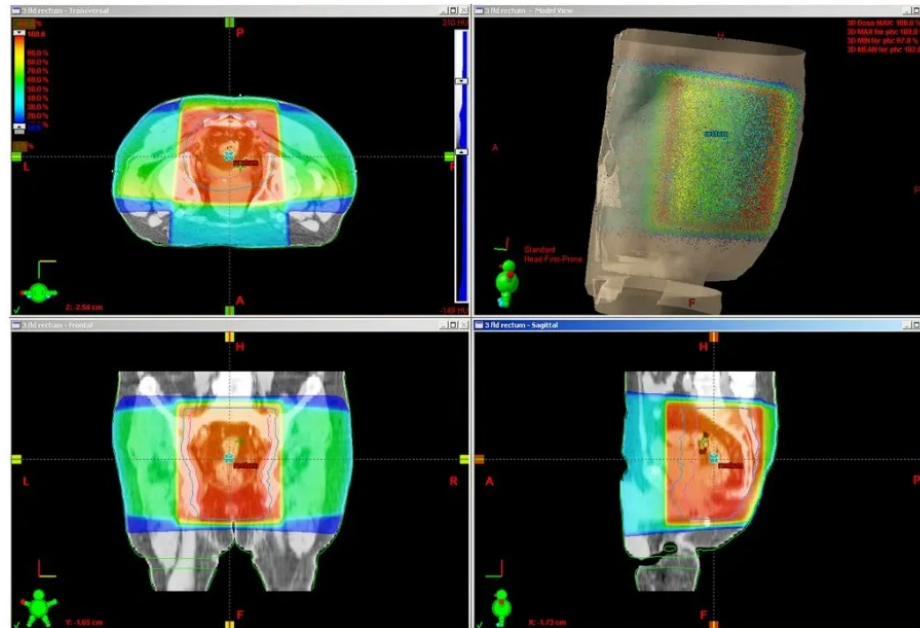
Relationships and commitments

Responsibilities

**New updates:
Omitting surgery / Organ preservation?**



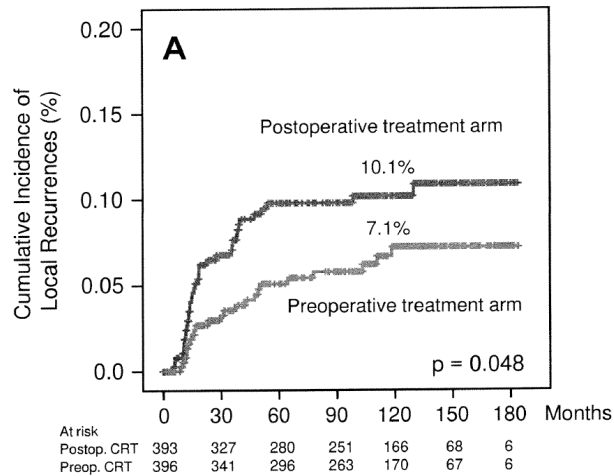
Rationale for Radiation



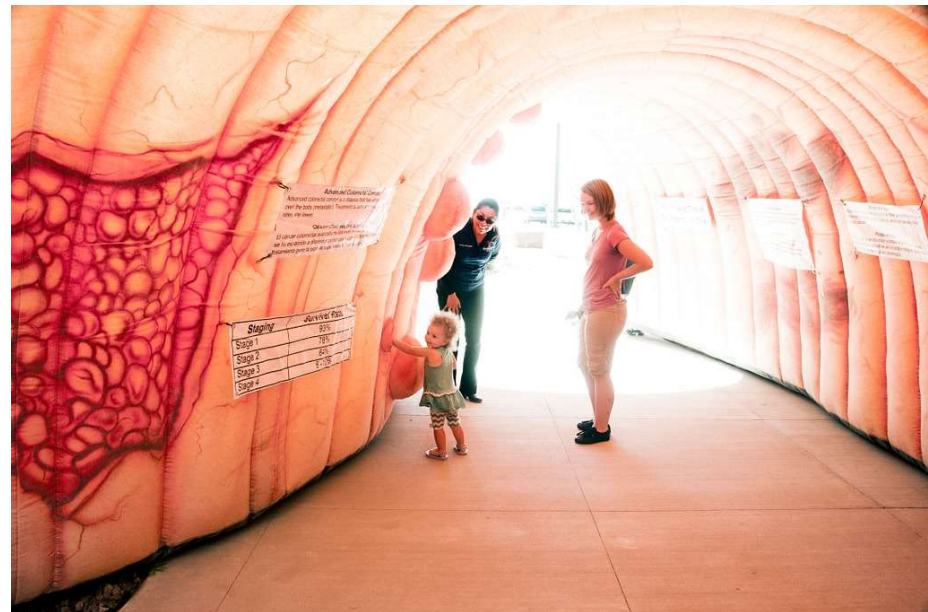
New York Times June 2023

- Radiate the rectal tumor and nearby lymph nodes
- To decrease the risk of “local” recurrence after surgery

Rationale for Radiation



Roedel et al JCO 2012



“Historical standard” for T3 and node+
Preoperative radiation with chemo (infusional 5FU or capecitabine) for 5 weeks
→ Surgery → Chemotherapy

Introduction

Review rationale: The 10,000 Ft. View

New updates: To Escalate or De-Escalate?

- 1) “Total neoadjuvant treatment” (TNT)**
- 2) Short course vs. long course radiation**
- 3) Omitting radiation**
- 4) Omitting surgery (“watch and wait”)**

New Updates: Escalate or De-Escalate?



One size does not fit all!

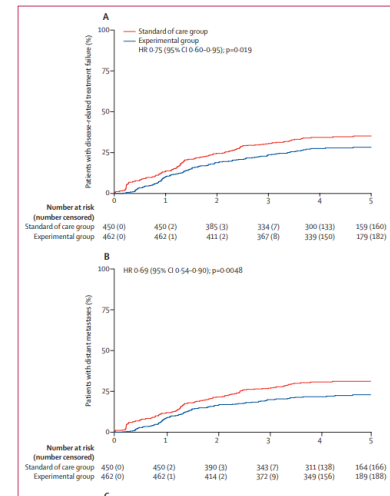
Total Neoadjuvant Therapy TNT 2020

- **RAPIDO trial:**
5 days of RT → Chemotherapy → Surgery
- **PRODIGE 23 trial:**
Chemotherapy → 5 weeks of RT → Surgery

* In patients with higher risk tumor features:

T4, vascular invasion, more lymph node burden

* Improved disease recurrence and distant metastases rates



Short vs. Long Course RT 2023

5 days of RT (RAPIDO) or 5 weeks (PRODIGE)?

10% local recurrence vs. 6% local recurrence



The
pendulum
has swung
back toward
“long course”

Long-Course is Preferred

- **Especially:**

- 1) **“Low” rectal tumor to help organ (sphincter) preservation**

- 2) **Watch and wait (surgery being omitted)**

- 3) **Anatomy, like prior hysterectomy**

Short Course Side Effects

- Overall short and long course radiation affect have similar side effects, for example on bowel movements, urination, and skin reaction, but the trajectory is very different.
- Usually *asymptomatic* the week of short course treatment
- 1 week after RT, diarrhea and urinary irritation, skin reaction.



De-Escalation: Omitting Therapies

Omitting Radiation

The New York Times



By [Gina Kolata](#)

Published June 4, 2023 Updated June 5, 2023

Rectal Cancer Patients Could Be Spared the Effects of Radiation

A large “de-escalation” trial suggests that tens of thousands of people annually may be able to rely on only chemotherapy and surgery to treat their illness.

Omitting Radiation





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ORIGINAL ARTICLE



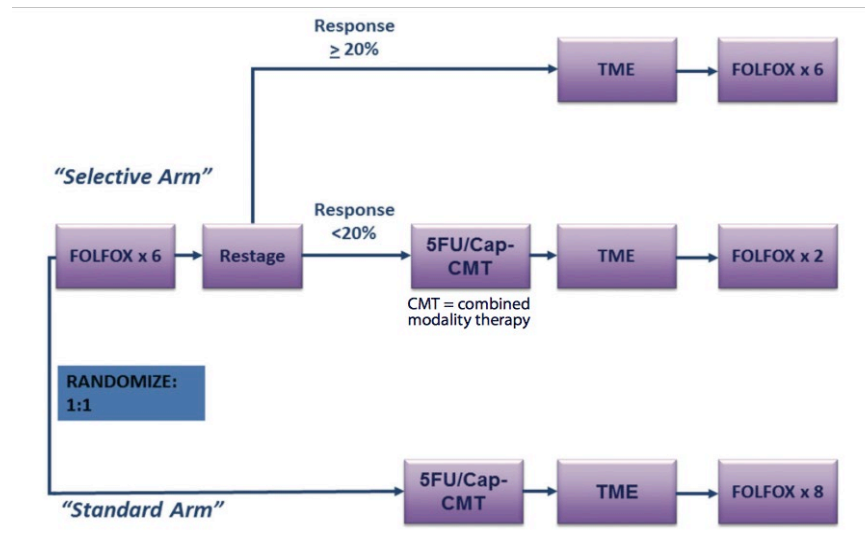
Preoperative Treatment of Locally Advanced Rectal Cancer

Authors: Deborah Schrag, M.D., M.P.H. , Qian Shi, Ph.D., Martin R. Weiser, M.D., Marc J. Gollub, M.D., Leonard B. Saltz, M.D., Benjamin L. Musher, M.D., Joel Goldberg, M.D., , and Harvey J. Mamon, M.D., Ph.D. [Author Info & Affiliations](#)

Published June 4, 2023 | N Engl J Med 2023;389:322-334 | DOI: 10.1056/NEJMoa2303269 | [VOL. 389 NO. 4](#)

PROSPECT Trial

T2N1, T3N0, T3N1, who are candidates for sphincter sparing surgery



**Chemo first, if good response go to surgery;
If no substantial response, RT then surgery**

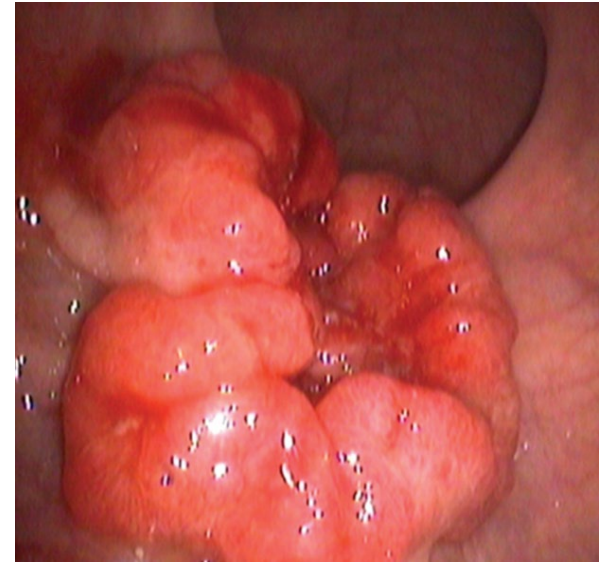
PROSPECT Trial

- **More than 1,100 patients**
- **Similar outcomes to the “historical standard”:
About 80% free of any disease at 5 years.**
- **Among those who went through initial chemo,
9% had to end up with radiation; 1.4% radiation
after surgery; ~90% successfully omitted
radiation.**

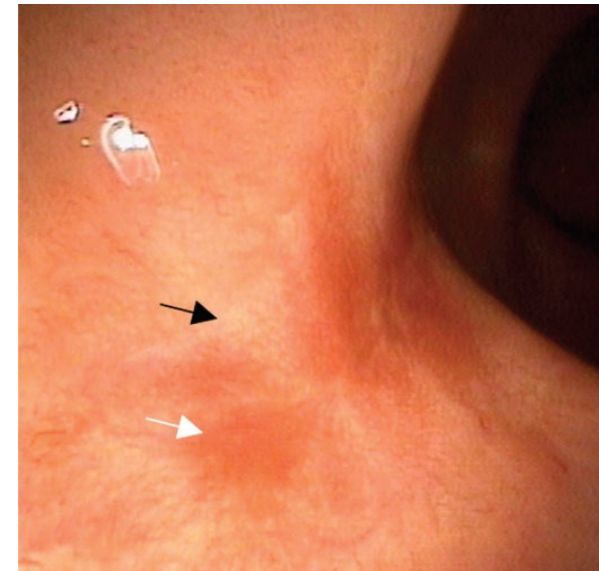
Watch and Wait: Omitting Surgery

- Growing recognition that response to preoperative treatments varies among patients/tumors
- Growing evidence that some patients who have a “complete clinical response” can sustain the response, without surgery.

Response A

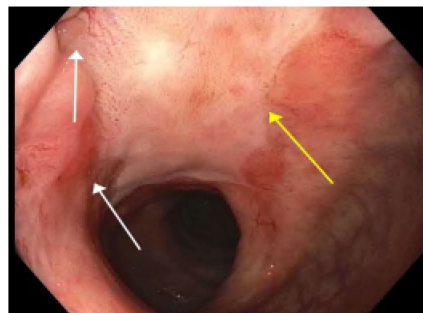
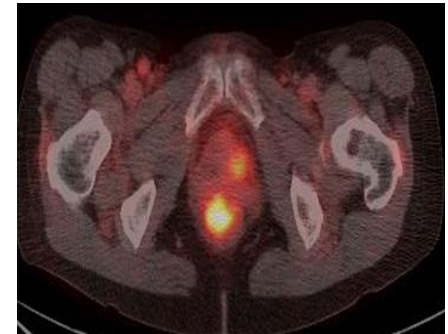
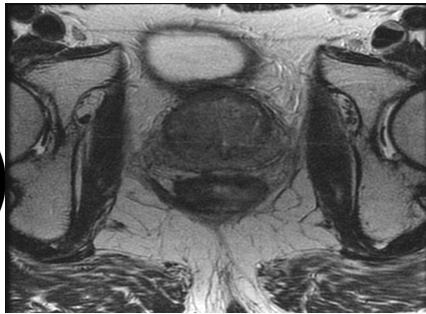
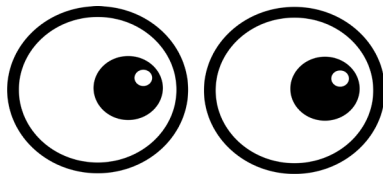


Response B



Judging Candidacy For Organ Preservation / W&W

Tests that assess response to neoadjuvant therapy



- No residual mass, ulceration, or stenosis
- Whitening of the mucosa
- Telangiectasia

Judging Candidacy For Organ Preservation / W&W

- **Ability to commit to systemic therapy and radiation & attendant toxicities**
- **Ability to commit to long-term surveillance & associated uncertainty, anxiety**
- **Willingness to accept the potential for failure**
 - **Local complications**
 - **Re-growth**
& subsequent course of action

Watch and Wait: Omitting Surgery

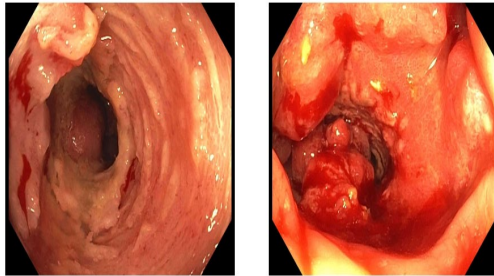
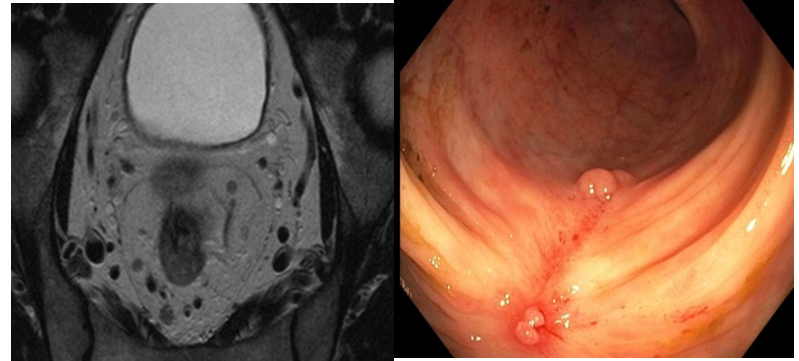
- **JANUS Clinical Trial Open Now:
Comparing triplet chemotherapy + RT vs
Doublet chemotherapy + RT
in Stage II to III rectal cancer**
- **5.5 to 6 weeks of radiation followed by chemo**

Judging Candidacy For Organ Preservation / W&W

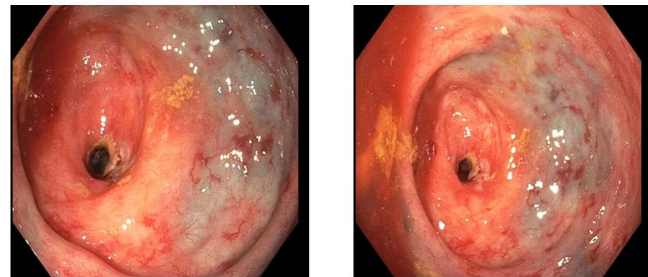


1. Locally perforated

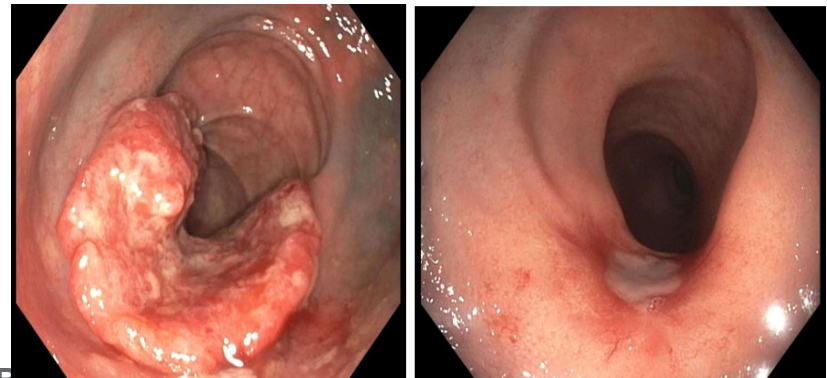
3. Not exactly complete clinical response



2. Strictured



4. Lost to Follow-up



Survivorship of Watch & Wait patients

Tasks of Cancer Survivorship Care (NCCN)

1. Surveillance for CRC recurrence
2. Management of treatment-related consequence
3. Prevention of second cancer / general health
4. Coordination of care within healthcare system

Generic	Cancer-specific
Negative feeling	Appearance concerns
Positive feeling	Financial problems
Physical pain	Distress over recurrence
Fatigue	Family-related distress
Social avoidance	Benefits of cancer
Cognitive problems	
Sexual problems	

Table 2: 12 domains examined by QLACS

Conclusions: Shared Decision-Making

One Size Does Not Fit All:

- **Do I have high risk features?
T stage, node involvement, EMVI, lateral nodes, close margin**
- **Do I have low risk features?**
- **Is long course or short course radiation best for me?**
- **Can I opt to omit radiation? Can I opt to omit surgery?**