

Young-onset Colorectal Cancer Virtual Patient Conference

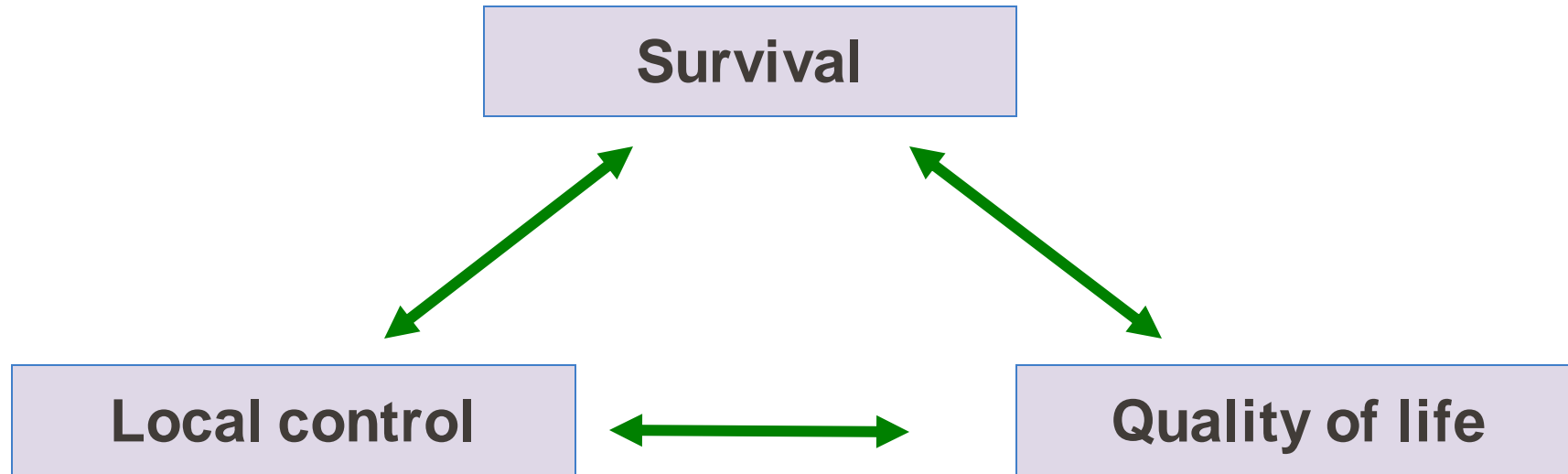
What is New in Young-onset Rectal Cancer

Outline

- **Goal of Treatment in Rectal Cancer**
- **Categorizing Rectal Cancer for Treatment Planning**
- **Personalizing Treatment For Optimal Outcome**

What is New in Young-onset Rectal Cancer

Goals of Treatment in Rectal Cancer



**Optimal surgery = Backbone
but not enough & major change in quality of life**

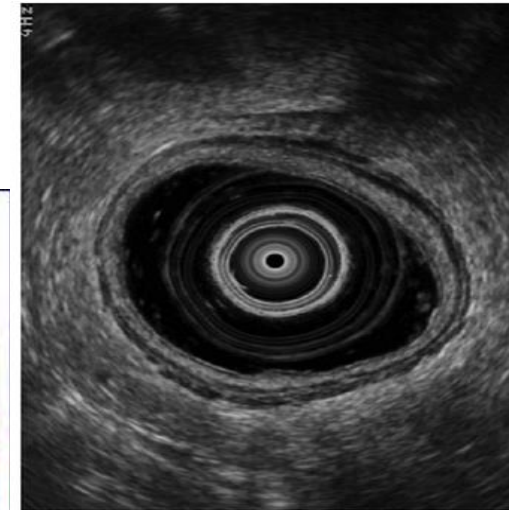
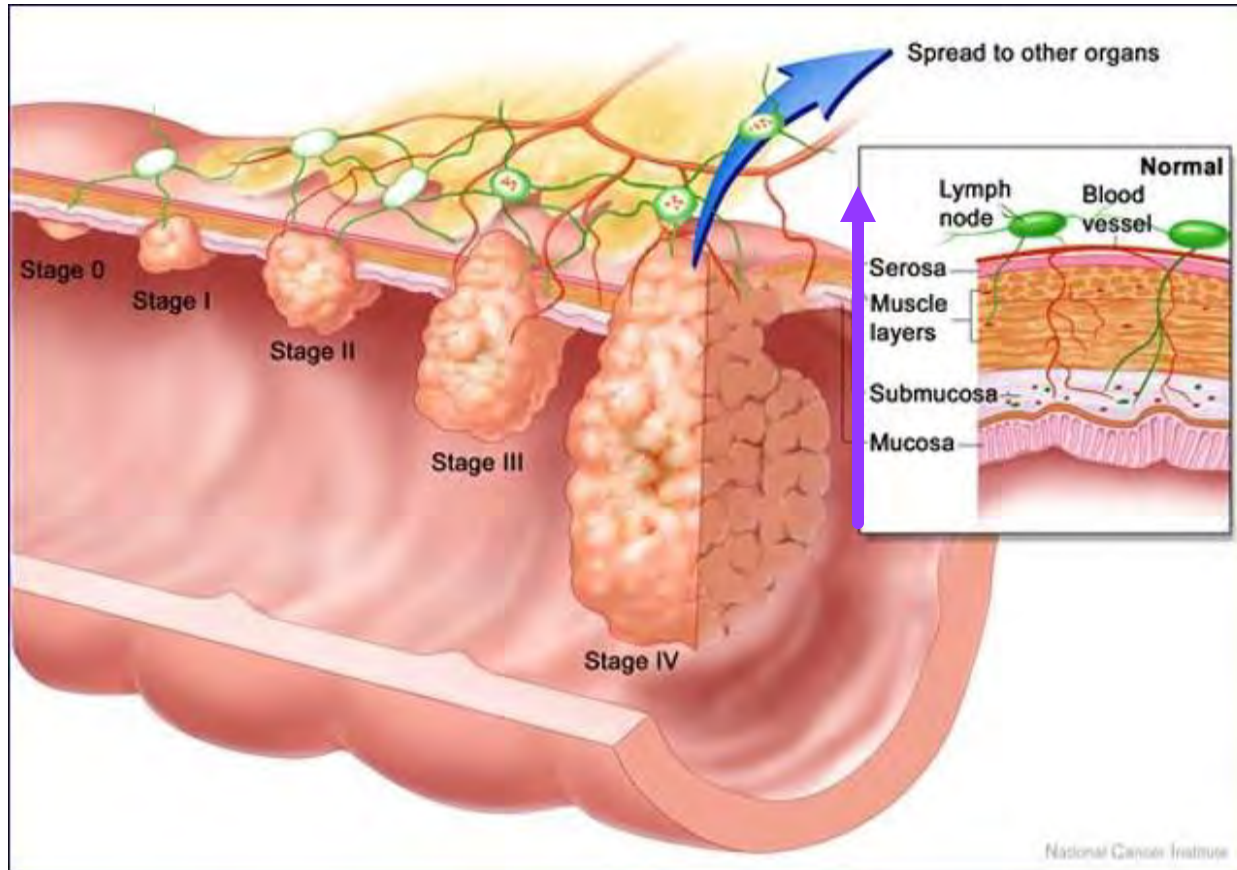
What is New in Young-onset Rectal Cancer

Categorizing Rectal Cancer for Treatment Planning

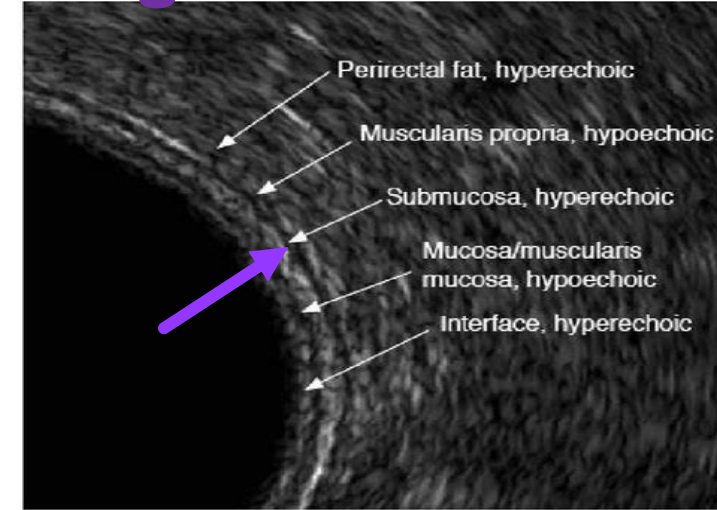
- **At diagnosis**
 - What is “Early” or “Locally-advanced”?
- **At follow-up**
 - Scanxiety : New tools for prognosis / surveillance ?

What is New in Young-onset Rectal Cancer

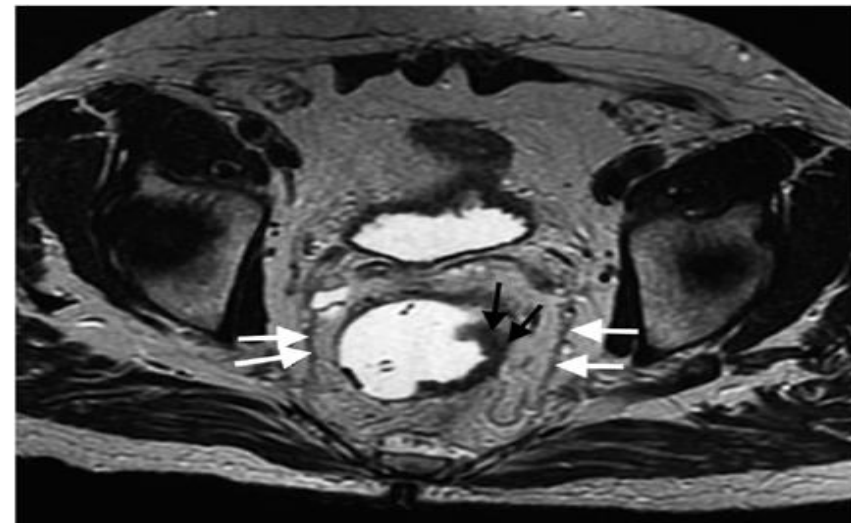
Categorizing Rectal Cancer for Treatment Planning



Optimal transrectal ultrasonography scan



Normal Rectal wall layers shown with ultrasonography

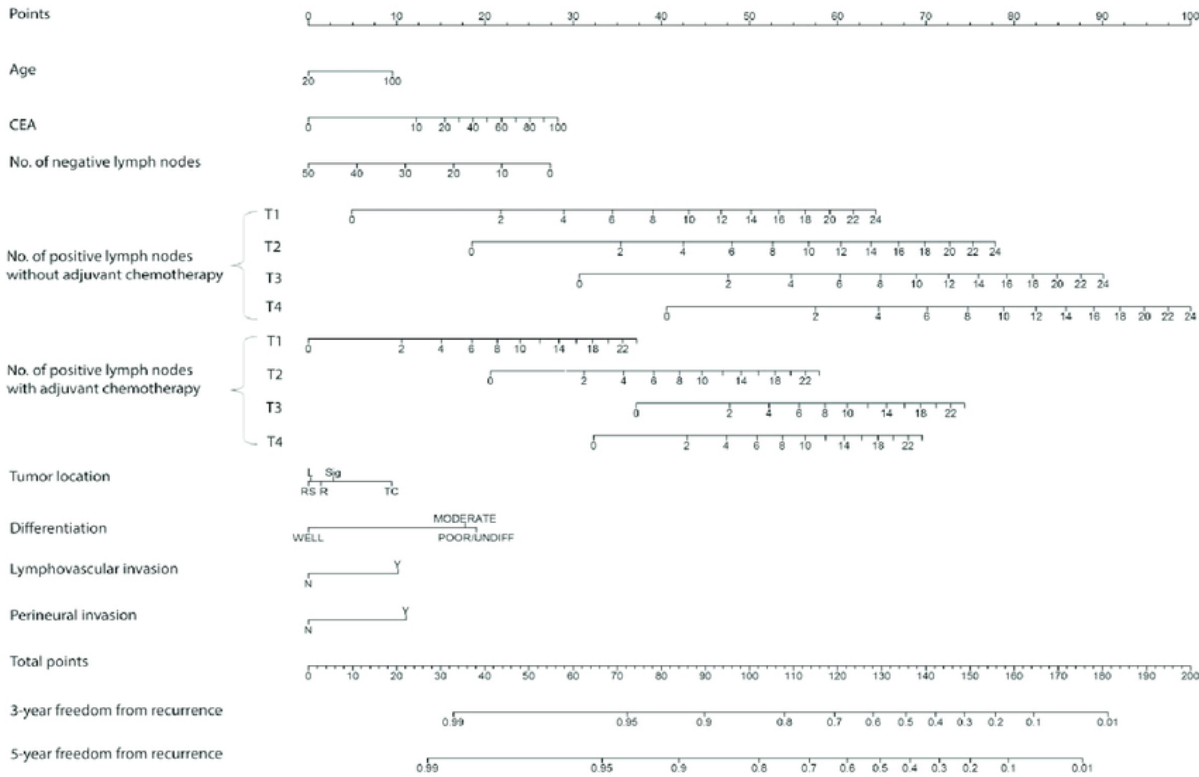


What is New in Young-onset Rectal Cancer

Categorizing Rectal Cancer for Treatment Planning

Scanxiety: Better tools?

MSKCC Nomogram; MDACC Conditional Survival Calculator



Rectal Cancer Survival Calculator

Choose the category that best describes the sequence of radiation therapy and surgical treatment patient received

pStage I-III No XRT
 ypStage I-III Pre-OP XRT
 pStage I-III Post-OP XRT
 Stage IV

Characteristics	Description
Age: <input type="text" value="<50"/>	The age of the patient at diagnosis
Sex: <input type="text" value="Male"/>	The sex of the patient
Race: <input type="text" value="White"/>	Patients race or ethnicity
Grade: <input type="text" value="Well and moderately differentiated"/>	The differentiation of the tumor cell
Stage: <input type="text" value="I"/>	The tumor stage according to American Joint Committee on Cancer staging system (v6)
Surgery: <input type="text" value="Local excision"/>	The primary surgery patient received

Report the year conditional survival

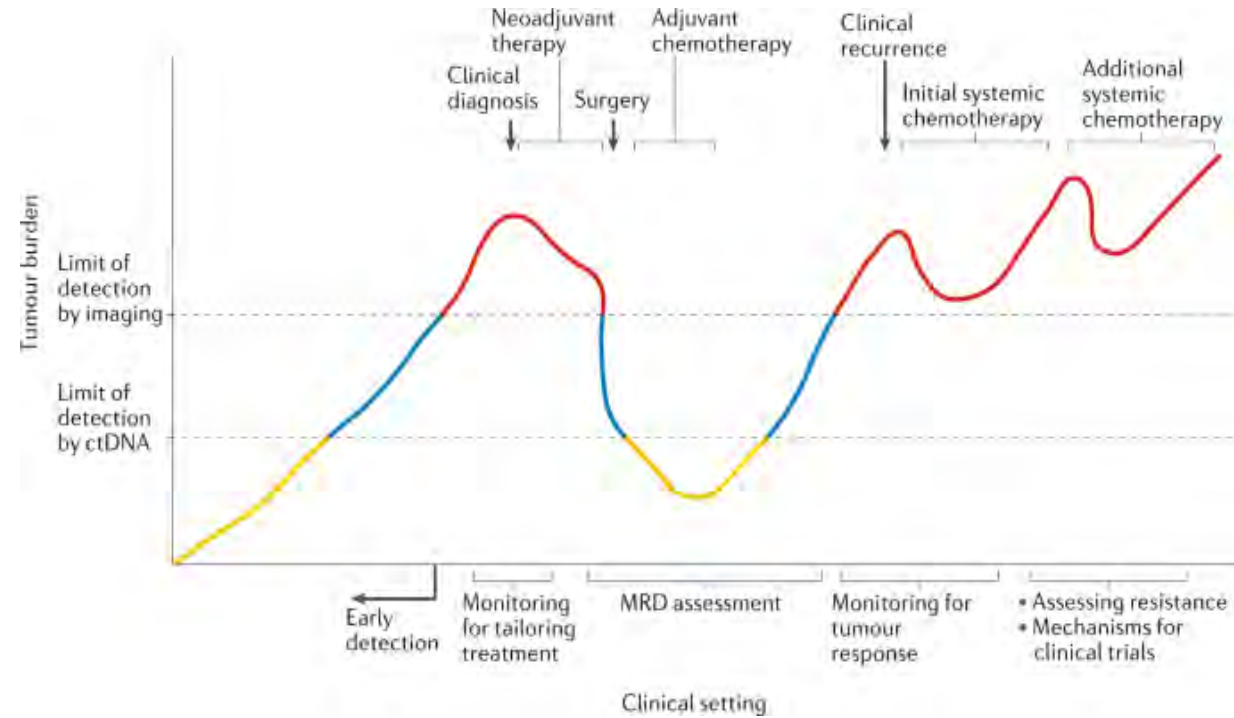
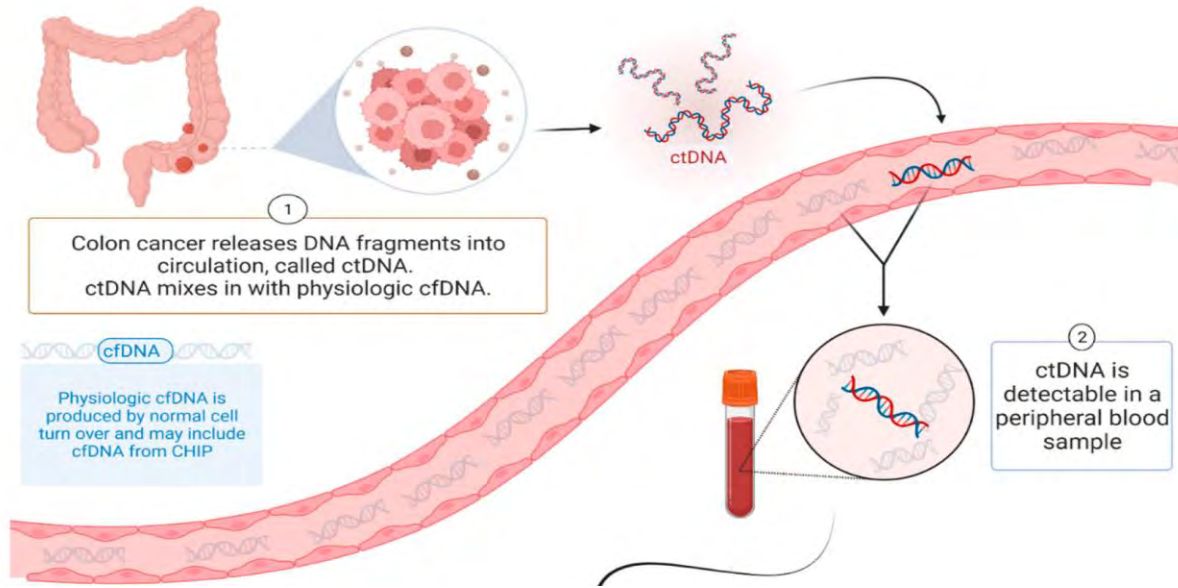
Disclaimer: This calculator is not meant to be a substitute for medical opinions by qualified physicians regarding cancer treatment. Results from this calculator should only be used in conjunction with all other clinical information in each case.

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Categorizing Rectal Cancer for Treatment Planning

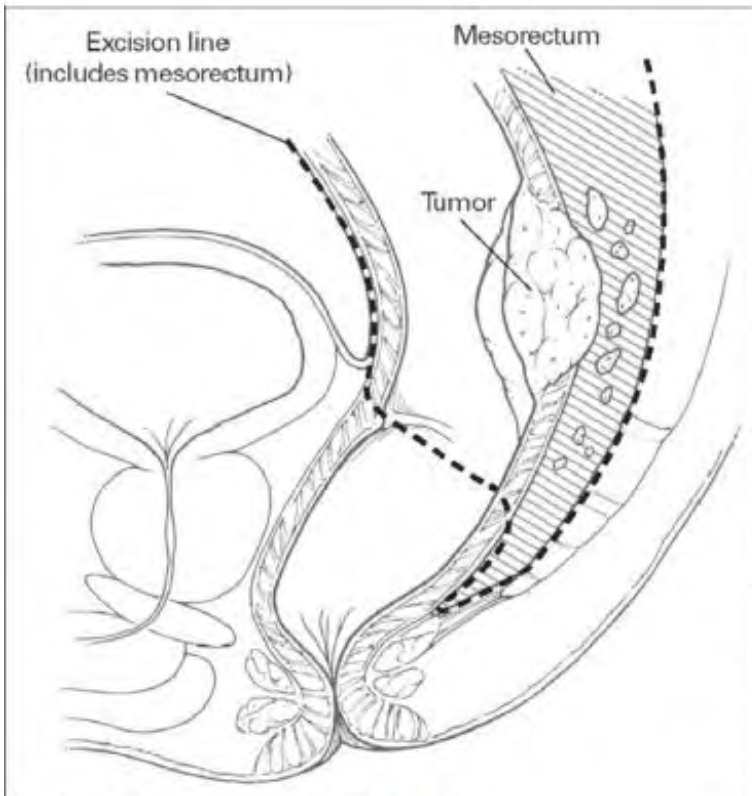
Scanxiety: Better tools?

ctDNA ?



What is New in Young-onset Rectal Cancer Personalizing Treatment For Optimal Outcome

Principles of Surgery For Optimal Local Control



**Total Mesorectal
Excision**



**Circumferential
Resection Margin
(CRM)**



**Regional
Lymphadenectomy**

What is New in Young-onset Rectal Cancer

Personalizing Treatment For Optimal Outcome

Impact on functions and quality of life

Low Anterior Resection Syndrome

Symptoms

-  Variable, unpredictable bowel function
-  Emptying difficulties
-  Altered stool consistency
-  Urgency
-  Increased stool frequency
-  Incontinence
-  Repeated painful stools
-  Soiling

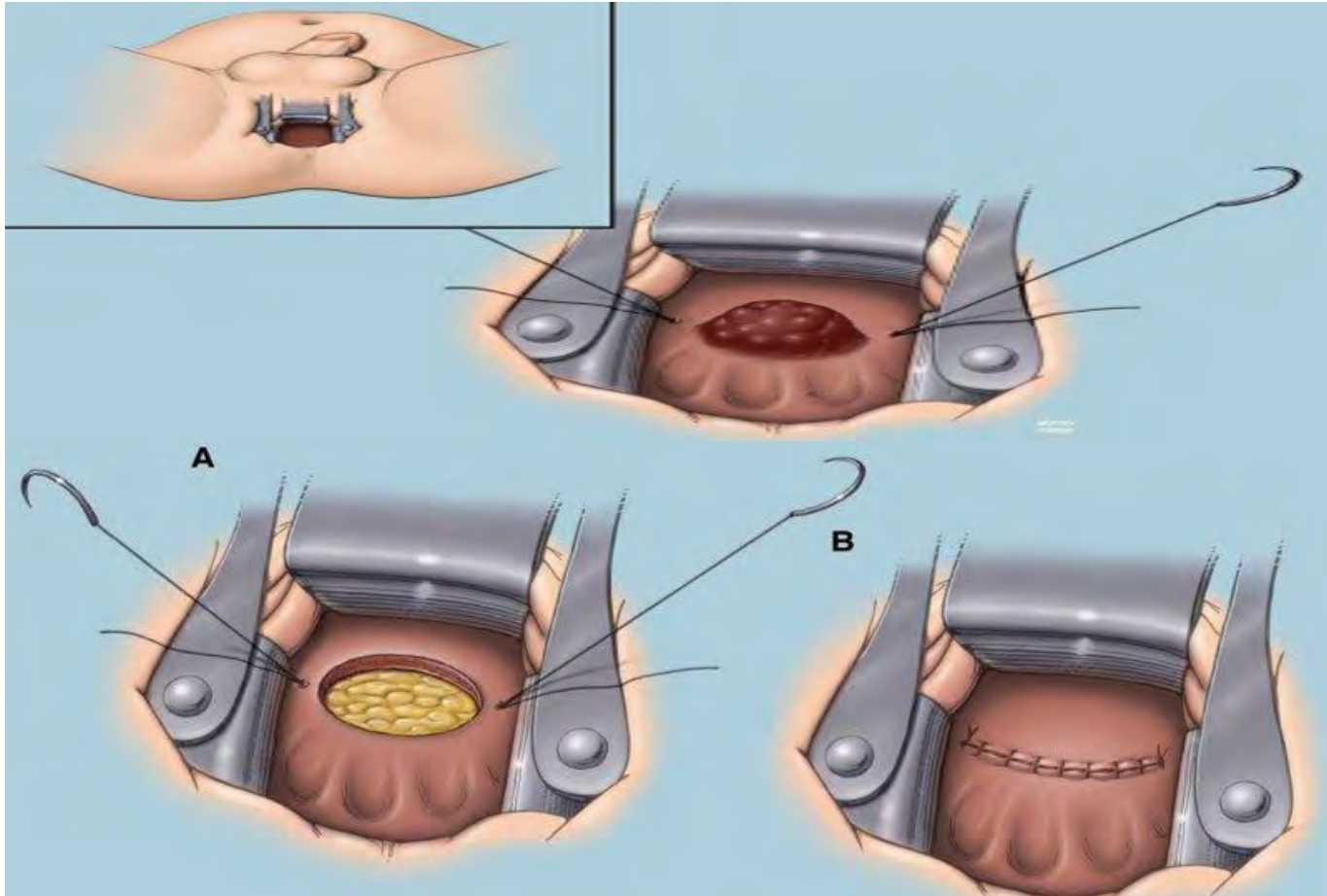
Consequences

-  Toilet dependence
-  Preoccupation with bowel function
-  Dissatisfaction with bowels
-  Strategies and compromises
-  Impact on: Mental and emotional wellbeing
-  Social and daily activities
-  Relationships and intimacy
-  Roles, commitments and responsibilities

What is New in Young-onset Rectal Cancer

Personalizing Treatment For Optimal Outcome

Local excision of Rectal Cancer: When is it safe to not remove more rectum or lymph nodes?



- Early T1
- Favorable features

What is New in Young-onset Rectal Cancer Personalizing Treatment For Optimal Outcome

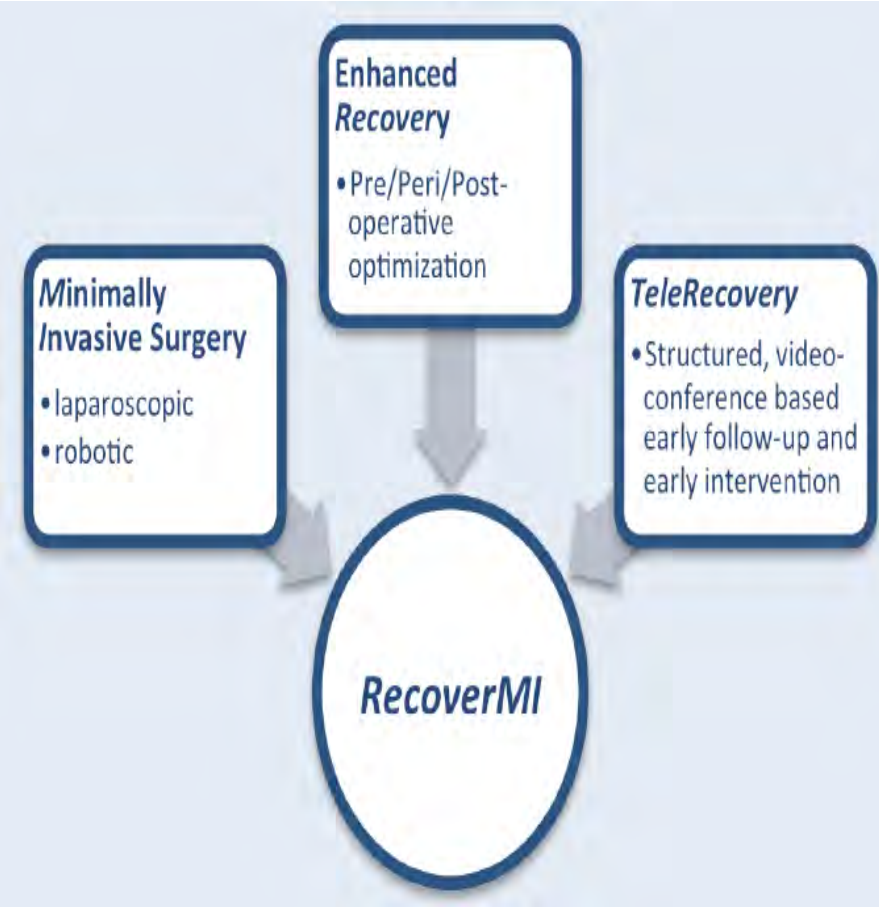
Local excision of Rectal Cancer: Can we “convert” some tumors to be “safe”?

- ACOSOG Z6041



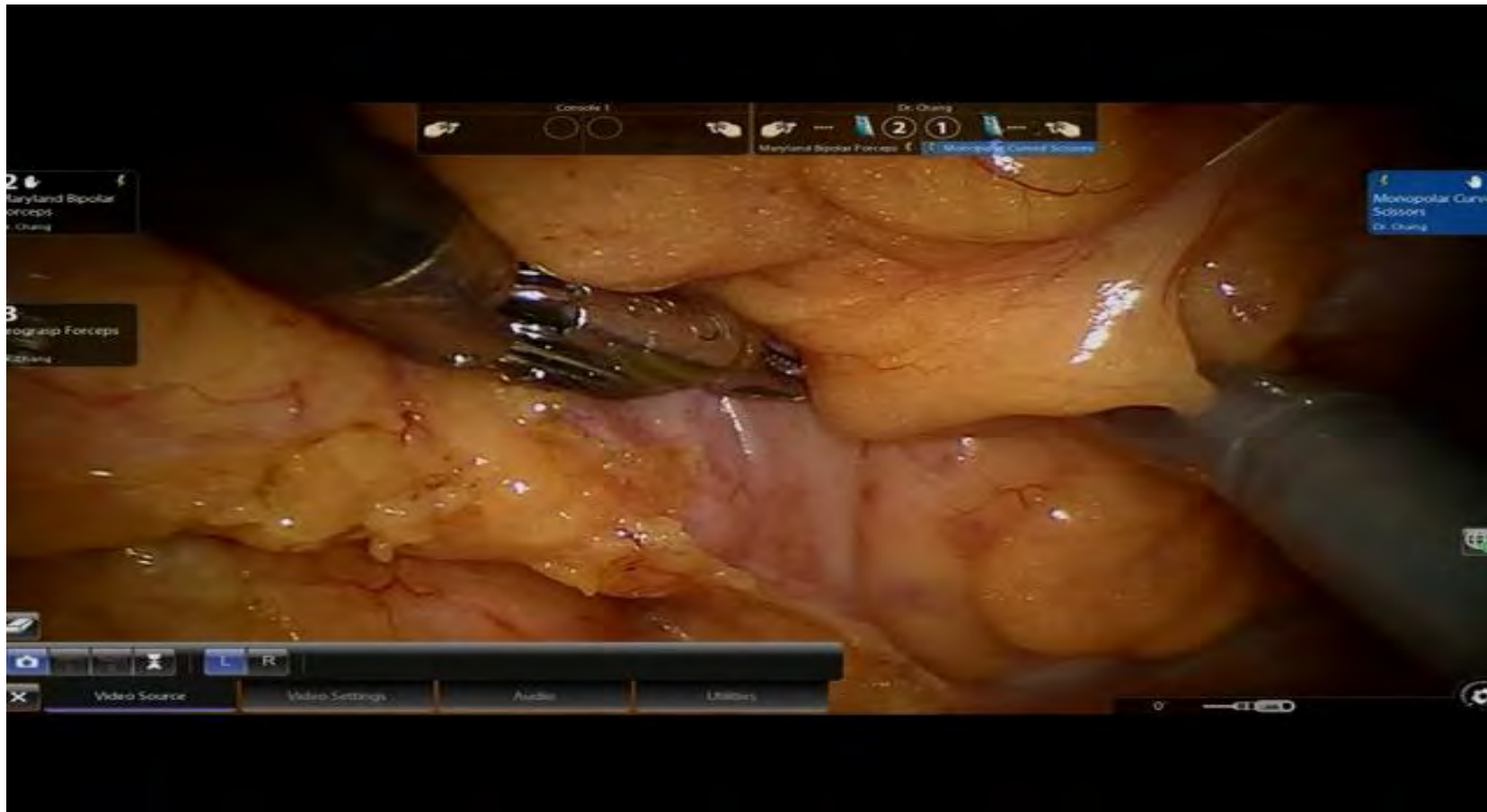
What is New in Young-onset Rectal Cancer Personalizing Treatment For Optimal Outcome

Let's make the surgery experience better !



What is New in Young-onset Rectal Cancer Personalizing Treatment For Optimal Outcome

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What is New in Young-onset Rectal Cancer

Personalizing Treatment For Optimal Outcome

Goals of treatment of Locally Advanced Rectal Cancer

- Prevent distant (metastatic) recurrence
- Prevent Local-regional (pelvic) recurrence
- Individualize therapy
 - Omission of surgery
 - Omission of radiation
 - Biomarker driven approach: dMMR/MSI

What is New in Young-onset Rectal Cancer

Individualizing Therapy in Locally Advanced Rectal Cancer

Omission of radiation

- Do all locally advanced rectal cancers *need* to be radiated
 - Location matters
 - Response to systemic therapy matters (biomarker driven intensification of therapy)

What is New in Young-onset Rectal Cancer

Individualizing Therapy in Locally Advanced Rectal Cancer

Omission of radiation

- WHY?

Associated with significant short and long term toxicity
--bowel, bladder, sexual dysfunction, infertility

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Individualizing Therapy in Locally Advanced Rectal Cancer

Omission of radiation

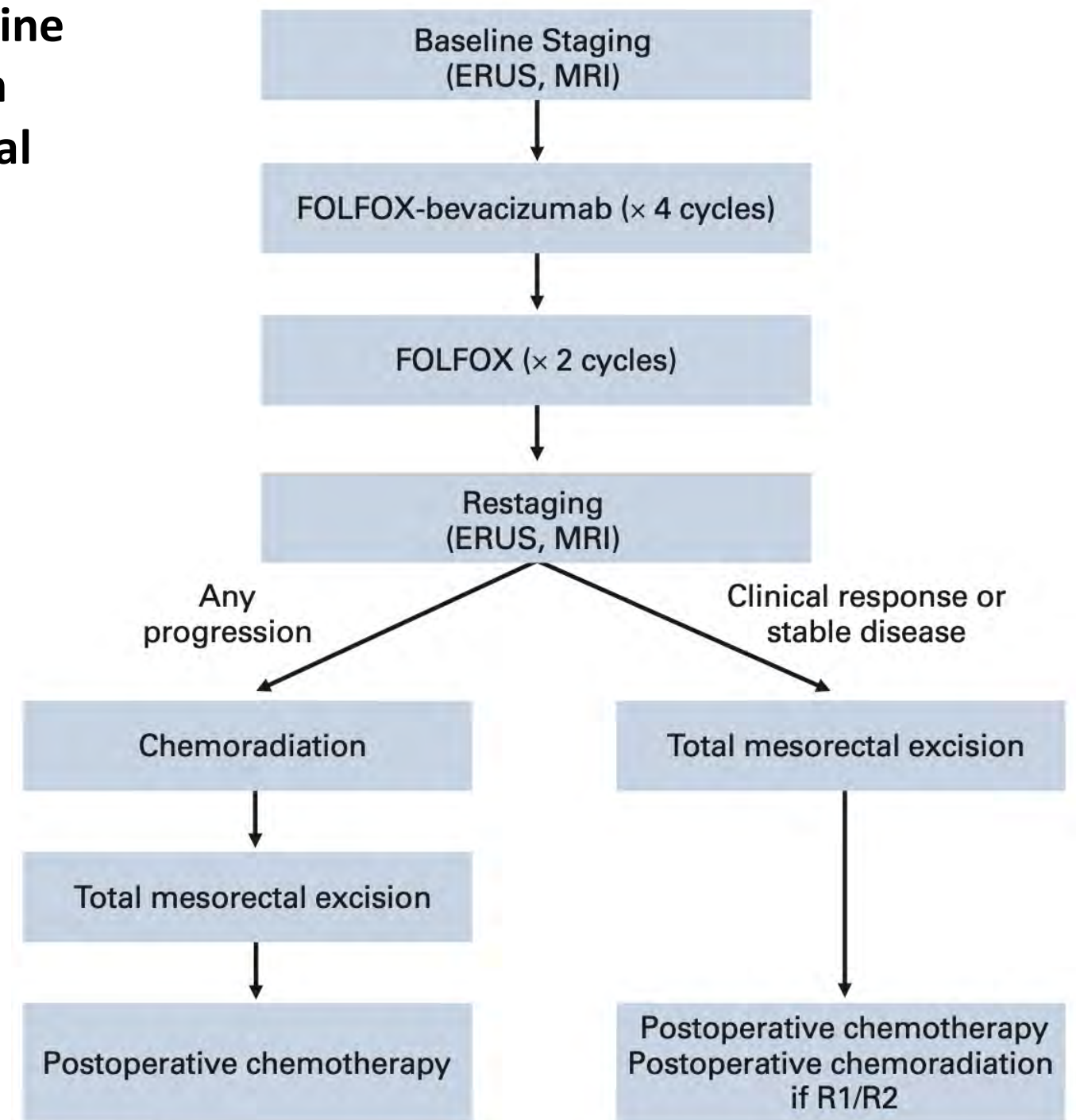
- Historical data supports benefit of RT for local pelvic control, no survival benefit
- Data from metastatic disease notable for significant responses to chemotherapy in primary, without need for surgery or RT

Neoadjuvant Chemotherapy Without Routine Use of Radiation Therapy for Patients With Locally Advanced Rectal Cancer: A Pilot Trial

Stage II/III rectal cancer
cT3N0/N+
Candidates for LAR

Ineligible:
T4
unresectable

Schrag D.,Saltz L., JCO 2014



Neoadjuvant Chemotherapy Without Routine Use of Radiation Therapy for Patients With Locally Advanced Rectal Cancer: A Pilot Trial

N= 32 patients

- 22 Node +

30 completed neoadjuvant therapy

3 recurred, lung mets

Table 1. Summary of Study Outcomes With Mean of 53 Months of Follow-Up Since Enrollment

Study Outcome	No.	%	95% CI
R0 resection rate	32	100	89 to 100
Pathologic complete response rate	8	25	11 to 43
Completion of neoadjuvant FOLFOX/bevacizumab	30	93.8	79 to 99
Preoperative chemoradiation	2	6.3	1 to 21
Postoperative radiation	1	3.1	1 to 16
4-year local recurrence rate	0	0	0 to 11
4-year disease-free survival	27	84	67 to 94
4-year overall survival rate	29	91	75 to 98

Abbreviation: FOLFOX, infusional fluorouracil, leucovorin, and oxaliplatin.

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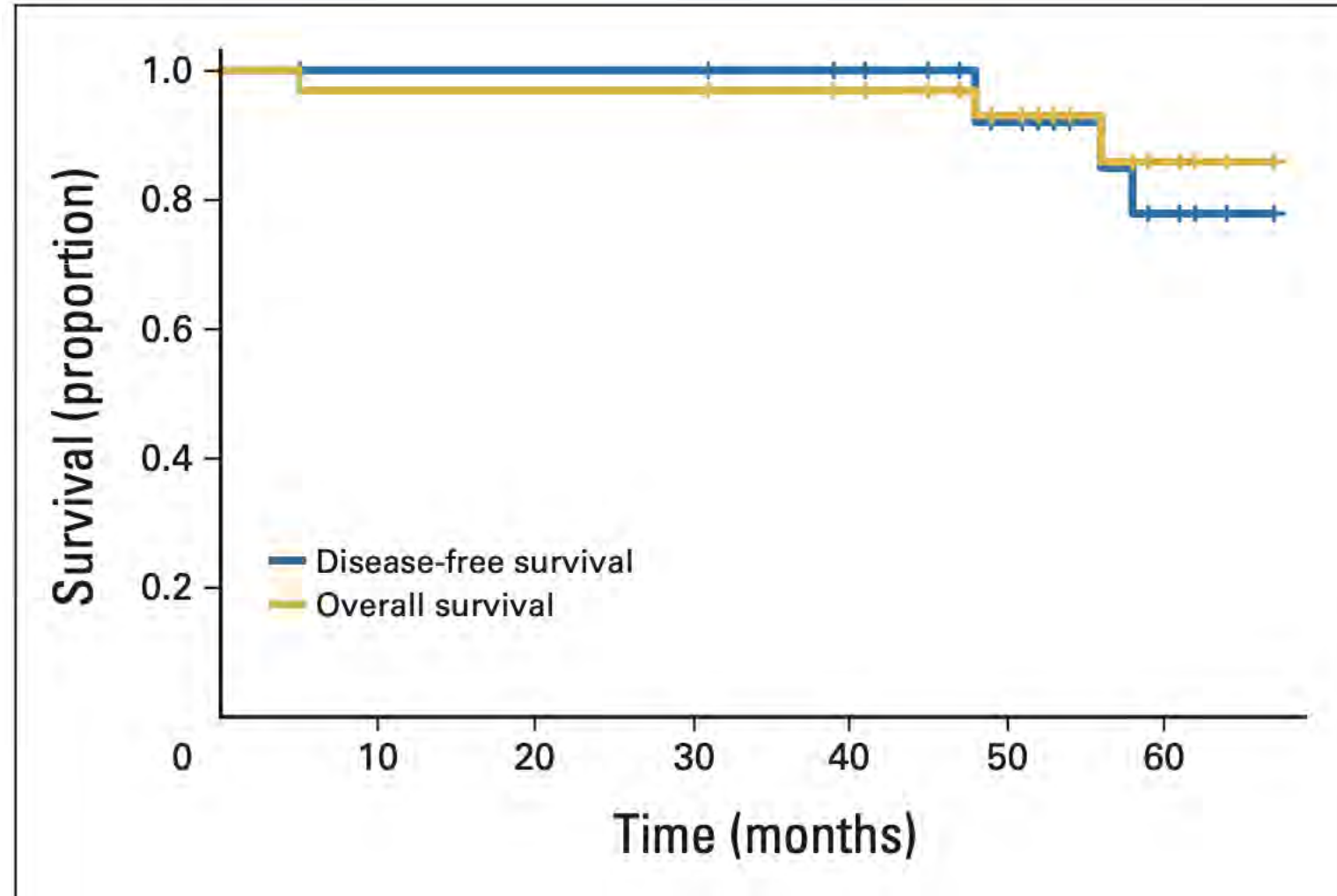
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PROSPECT

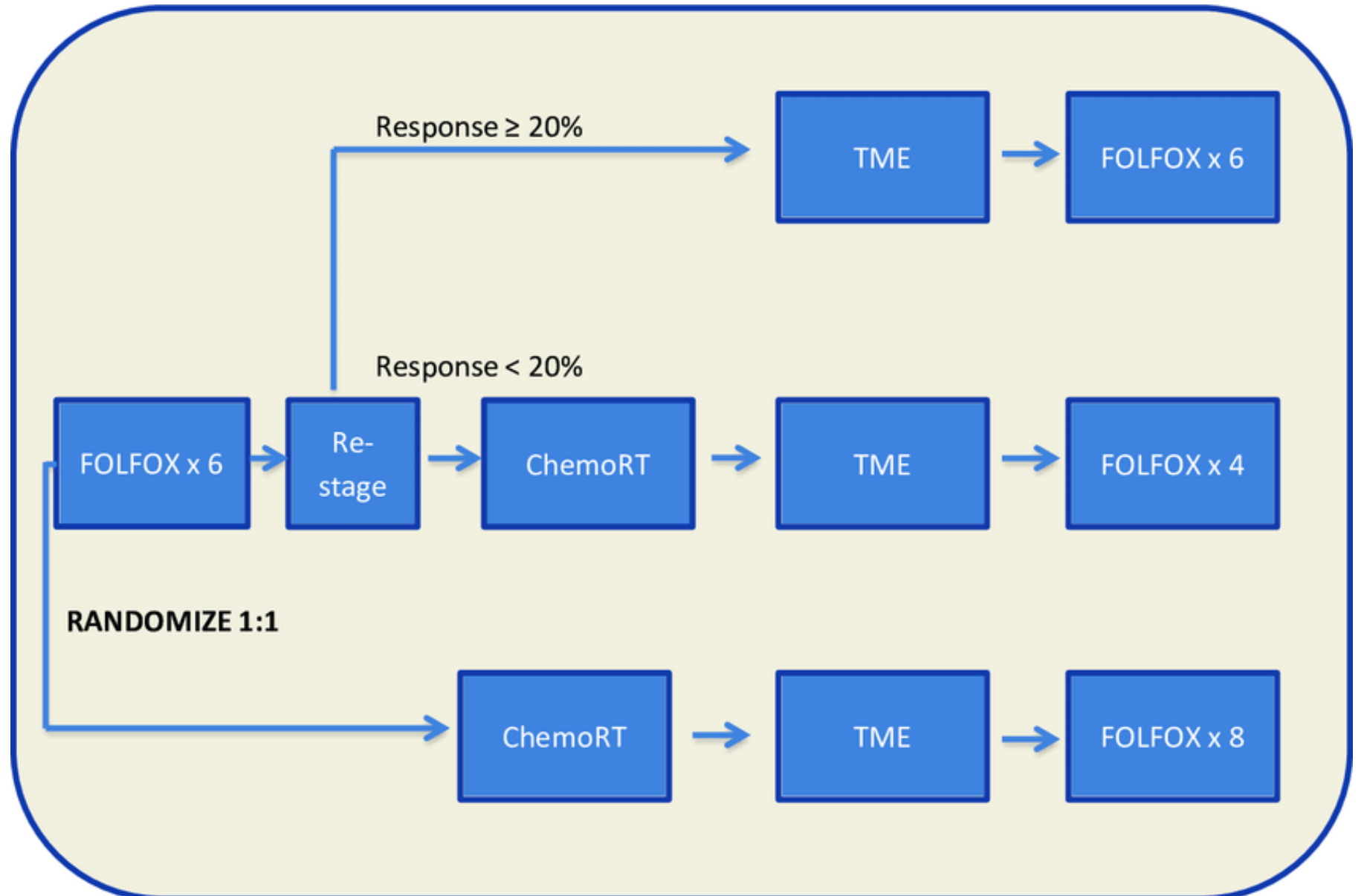
- N= 1100
- Rectal adeno
- T21
T3N0-2
- Candidate for sphincter sparing surgery

Primary Objective:

- R0 resection, noninferiority TLR
- DFS

Secondary Objectives:

- TLR rates
- pCR rates
- OS



PROSPECT



Data will be presented at ASCO 2023!!

Individualizing Therapy in Locally Advanced Rectal Cancer

- Do all locally advanced rectal cancers *need* to be radiated
 - Location matters
 - Response to systemic therapy matters
 - Biomarker driven therapy can improve neoadjuvant responses

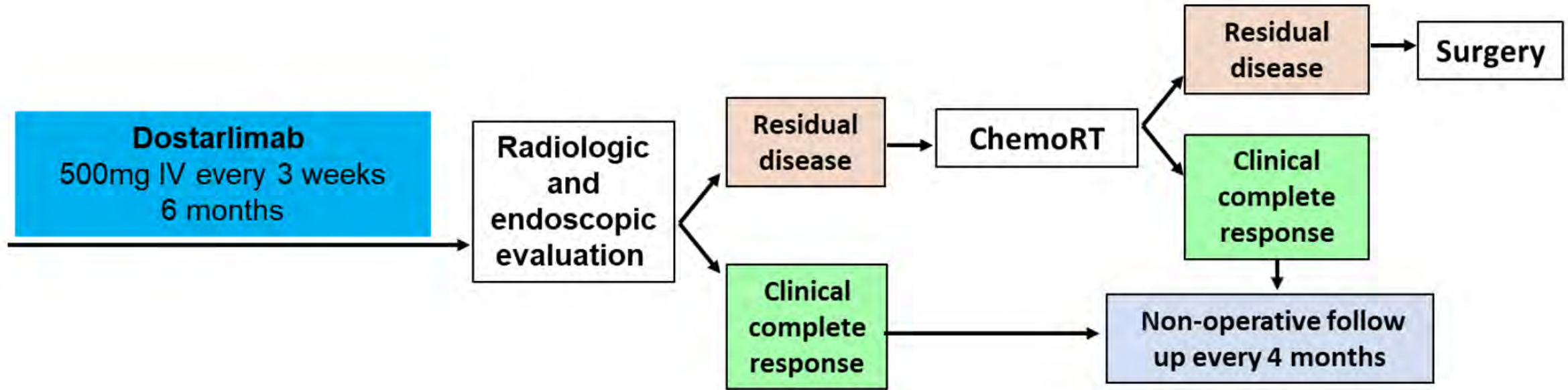
Locally Advanced Mismatch Repair Deficient Rectal Cancer

- About 5-10% of all rectal cancers
- Less sensitive to chemotherapy
 - Adjuvant therapy
 - Neoadjuvant rectal - TNT

Outcome	No. of patients (%)	
	dMMR	pMMR
FOLFOX as initial treatment	<i>n</i> = 21	<i>n</i> = 63
Progression of disease	6 (29)	0
Response or stable disease	15 (71)	63 (100)
Chemoradiation as initial treatment	<i>n</i> = 16	<i>n</i> = 48
Progression of disease	0	0
Complete pathologic response	2 (13)	8 (17)

- Checkpoint blockade is highly effective in metastatic mismatch repair-deficient cancers with a complete response rate ~10%

Phase II study of neoadjuvant PD-1 blockade in MMRd locally advanced rectal cancer



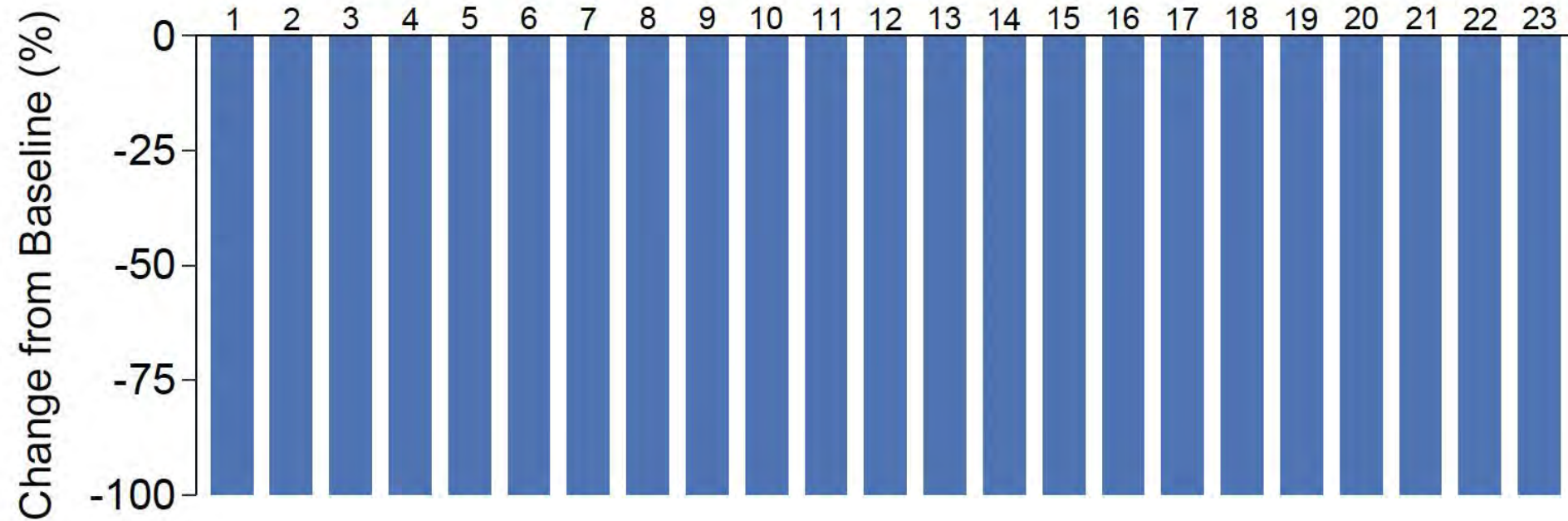
Patient population: Stage II and III mismatch repair-deficient rectal cancer

Target Enrollment: 30 subjects

Study Design: Simon's 2-stage minimax design

Responses

patients who completed dostarlimab N=23



Conclusion

Treatment of locally advanced rectal cancer should be individualized

Selective omission of radiation is feasible
depending on tumor location
response to neoadjuvant chemotherapy

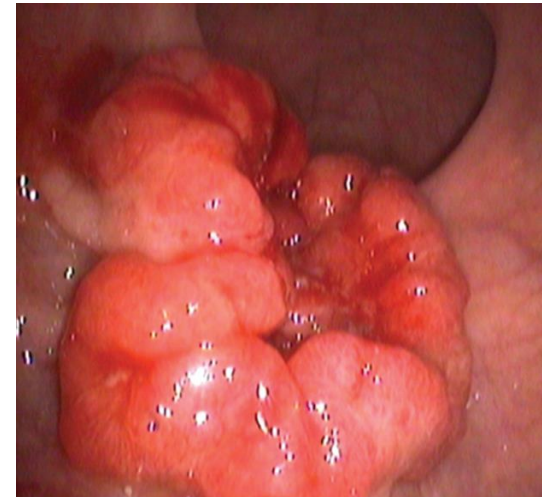
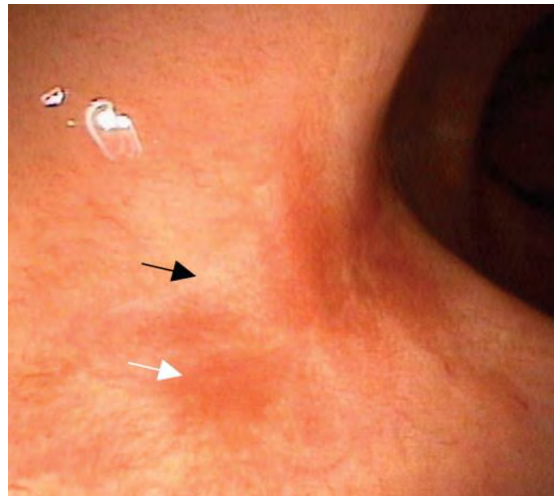
Biomarker driven neoadjuvant therapy such as PD-1 blockade in mismatch repair deficient tumors can improve responses and potentially replace chemotherapy, radiation and surgery

What is New in Young-onset Rectal Cancer Personalizing Treatment For Optimal Outcome

When There is A Complete Clinical Response

When is it safe to Watch & Wait, Maximizing Response, Follow-up, Salvage

- Digital Rectal Exam
- MRI
- Endoscopy



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Thank You!!