

radiation therapy for lower gastrointestinal malignancies

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locally advanced rectal cancer LARC

new emerging data that may change daily clinical practice

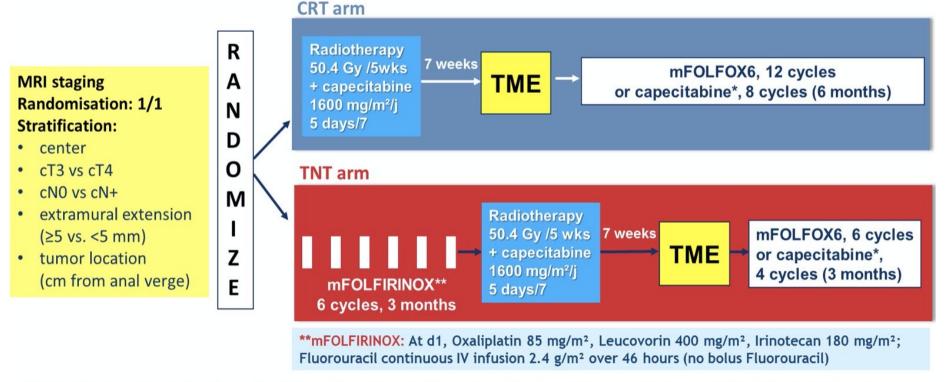
total neoadjuvant therapy

Total Neoadjuvant Therapy

- distant recurrence rates now exceed local recurrence rates
- move systemic therapy upfront to address micrometastatic disease earlier
- particularly in high-risk patients

PRODIGE 23 trial: study design

NCT 01804790; EudraCT 2011-004406-25



^{*}according to center choice throughout the study; adjuvant chemotherapy was mandatory in both arms regardless of ypTNM stage.

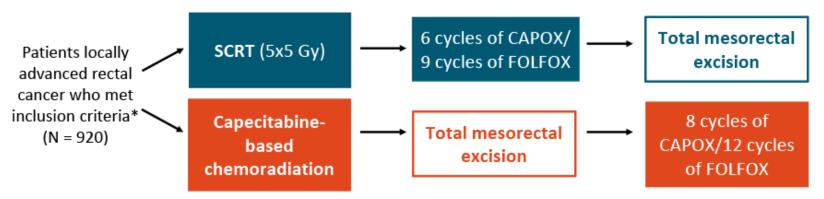
PRODIGE 23 trial: results

NCT 01804790; EudraCT 2011-004406-25

Endpoint	Modified FOLFIRINOX Followed by Chemoradiotherapy	Chemoradiotherapy	Hazard Ratio; P Value
3-year disease-free survival	75.7%	68.5%	0.69; P=.034
3-year metastasis-free survival	78.8%	71.7%	0.64; P = .017
Noncurative surgery	0%	3.7%	P=.007
Pathologic complete response (ypT0N0)	27.8%	12.1%	P < .001
Grade 3 or 4 adverse events with adjuvant chemotherapy	44.4% (3 months of chemotherapy)	52.5% (first 3 months of chemotherapy)	P = .03
6/25		74.1% (total 6 months of chemotherapy)	P < .001

RAPIDO: Preoperative Short-Course Radiotherapy and Chemotherapy for Locally Advanced Rectal Cancer

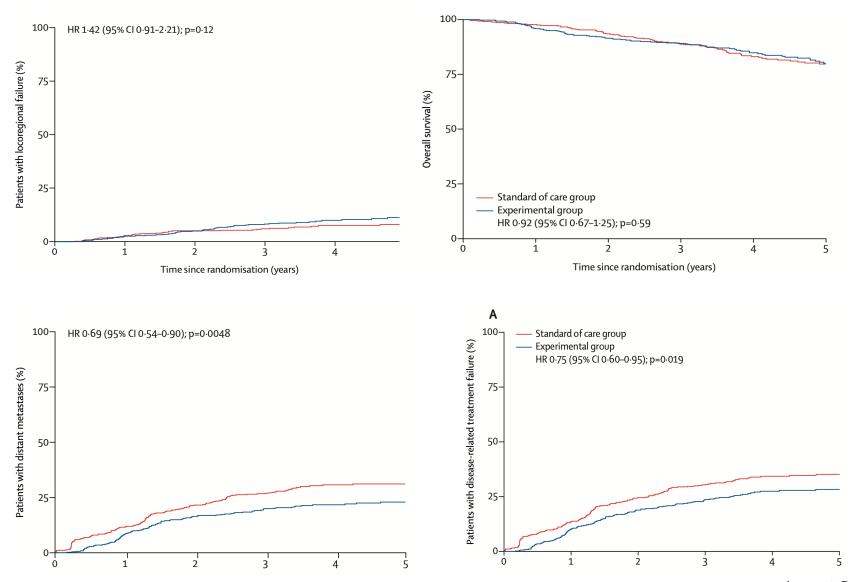
Randomized, international, multicenter phase III trial



^{*}Inclusion criteria: biopsy-proven primary adenocarcinoma of the rectum, 18 years or older, absence of distant metastases, MRI with high-risk features (T4a/b, extramural vascular invasion +N2, mesorectal fascia + enlarged lymph nodes).

- Primary endpoints: disease-related treatment failure
- Secondary endpoints: OS, R0 rate, pCR, toxicity, surgical complications, QoL at 3 yrs

RAPIDO: Preoperative Short-Course Radiotherapy and Chemotherapy for Locally Advanced Rectal Cancer





Outcomes	RAPIDO	PRODIGE 23
	(TNT vs. CRT)	(TNT vs. CRT)
Median FU	4.6 yrs	3.8 yrs
Primary endpoint	3-yrs DrTF	3-yrs DFS
	23.7% vs. 30.4% (HR 0.75 [95% CI 0.60–0.96]; p = 0.019)	75.7% vs. 68.5% (HR 0.69 95% [CI 0.49–0.97]; <i>p</i> = 0.034)
3-year MFS	80% vs. 73.2%	78.8% vs. 71.7%
pCR rate	28.4% vs. 14.3%	27.5% vs. 11.7%
Local relapse	8.7% vs. 5.4%	4.8% vs. 7%
3-year OS	89.1% vs. 88.8%	90.8% vs. 87.7%