positivity may correlate with the CPIs effectiveness. Nonetheless, it is currently unclear if adding CPIs to TNT in LARC impacts patients' long-term outcome.

Trial design: TOTAL is a prospective, multi-center, double arm, open-label, phase II randomized (1:1) controlled trial aimed to determine the efficacy and safety of adding tislelizumab to TNT in pts with LARC. Randomization is stratified by trial site and CPS ($\geq$1 or $<$1). Pts are treated by capecitabine-based CRT followed by 8 cycles of mFOLFOX, with or without tislelizumab. Pts are re-staged 8 weeks after treatment completion. Those who achieve predefined clinical CR/near CR will be followed closely by WW, and will undergo TME at any evidence of tumor regrowth. Pts with residual tumor will undergo immediate TME. We plan to enroll 134 pts within 12-14 months in 10 sites in Israel and Germany. Currently, 32 pts have been accrued. The trial's primary endpoint is 3-year TME-free survival; the sample size was planned to achieve 80% power to detect a 20% increase in 3-year TME-free survival rate, from 50% to 70%, with one-sided alpha=0.05. The study has several secondary endpoints: clinical, QoL and translational.

Clinical trial identification: NCT06940388 EU Clinical trial number: 2025-522120-28-00.

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331TiP GYNECARE-RT: Gynecologic care and sexual function preservation in women undergoing pelvic radiotherapy for colorectal and anal cancer

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Background: Pelvic chemoradiotherapy (C-RT) for colorectal and anal cancer may be related to genital and sexual toxicities, particularly in young women. Vaginal stenosis, dyspareunia, and sexual dysfunction may affect 30-80% of women. Despite high prevalence and available effective interventions, systematic gynecologic assessment and active measures remain largely absent from oncologic care. Evidence shows that structured gynecologic follow-up, vaginal dilators, and patient education can reduce RT-induced atrophy and preserve sexual function. However, prospective data are scarce, hindering evidence-based guideline development.

Trial design: Multi-cohort prospective observational study in women aged $>$65 years undergoing pelvic C-RT for rectal or anal cancer, comprising 3 cohorts: - Cohort A: Women 3-24 months post-RT, assessing late gynecologic toxicities, sexual dysfunction, and unmet supportive care needs. - Cohort B (Prospective): Newly diagnosed women undergoing gynecologic assessment at baseline, 1-, 3-, and 6-months post-RT, examining acute/late toxicity, sexual function, and QoL changes. - Cohort C (Interventional observational): Subset of Cohort B receiving vaginal dilators during and after RT, evaluating compliance, tolerability, and impact on vaginal stenosis versus non-users. Primary Objectives: - Incidence of genital toxicities $\geq$Grade 2 (CTCAE v5.0) at 6 months post-RT - Changes in sexual function (FSFI) from baseline to 6 months - Assess dilator compliance and impact on vaginal stenosis (Cohort C vs. B non-users). Secondary Objectives: - Characterize vulvovaginal symptom burden (VHI, VuHI) - Explore dose-volume relationships between pelvic organs and toxicity severity - Identify clinical and treatment predictors of worse sexual outcomes. Key Assessments: Gynecologic examination with Vaginal Health Index (VHI), Vulvar Health Index (VuHI), CTCAE toxicity, and PROMs including Female Sexual Function Index (FSFI) and EORTC QLQ-C30. Sample Size: Approximately 100 women across all cohorts for adequate precision in incidence estimation and multivariate exploratory analyses. The accrual began in March 2026 and is expected to be completed in approximately 24 months.

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332eP Pretreatment cell-free DNA as a biomarker of high-risk tumor biology in locally advanced and oligometastatic rectal cancer

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Background: Locally advanced rectal cancer is a heterogeneous disease and requires a risk-adapted approach. Elevated carcinoembryonic antigen (CEA) and high-risk MRI features (T4, mesorectal fascia involvement, $\geq$4 suspicious nodes, extramural venous invasion, lateral lymph nodes) are associated with inferior disease-free survival. Cell-free DNA (cfDNA) is an emerging biomarker that may identify patients at high risk of relapse who could benefit from intensified treatment. This study evaluates pretreatment total cfDNA levels and their association with tumor stage and prognostic factors.

Methods: Patients with stage II—III and oligometastatic stage IV rectal cancer (AJCC v.8) underwent comprehensive staging, including endoscopy, pelvic MRI, CT or PET/CT, and laboratory assessment including CEA. Plasma was collected prior to neoadjuvant therapy. cfDNA was quantified using fluorometry (Qubit) and capillary electrophoresis (Fragment Analyzer) to assess both concentration and the quality/fragmentation. Correlation between methods and association with stage and CEA were analyzed.

Results: Forty-nine patients were included (median age 67), including 8 stage II, 35 stage III, and 6 stage IV, all microsatellite-stable. cfDNA quantification showed strong concordance between methods (Pearson's $p<0.0001$). Baseline cfDNA positively correlated with CEA (Qubit $p<0.05$). Patients with advanced disease (stage IIIC—IV; n=15) had significantly higher pretreatment cfDNA than stage IIA—IIIB (n=34) (mean 1.11 vs. 0.68 ng/µl; range 0.52—1.70 vs. 0.26—1.20 ng/µl; $p<0.001$). Elevated cfDNA was associated with higher tumor burden and oligometastatic disease.

Conclusions: Pretreatment cfDNA levels correlate with tumor stage, CEA, and disease burden, supporting its potential as a noninvasive biomarker for risk stratification and selection of patients for intensified neoadjuvant therapy. cfDNA quantification using complementary methods is reliable and informative of high-risk tumor biology.

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333eP Prognostic significance of postoperative pathological features after neoadjuvant chemoradiotherapy in locally advanced rectal cancer

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Background: Standard treatment for locally advanced rectal cancer (LARC) includes neoadjuvant chemoradiotherapy (nCRT), followed by total mesorectal excision or a watch-and-wait (W&W) approach. Identification of prognostic markers is essential for optimizing treatment and personalizing patient management. This study evaluated prognostic parameters associated with disease-free interval (DFI) after nCRT using a simultaneous integrated boost (SIB).

Methods: This study included 82 patients treated from June 2020-April 2022. RT was delivered with 45 Gy to mesorectum and regional lymphatics, with a SIB to 54 Gy to the primary tumor (2.16 Gy/fr). Concomitant chemotherapy with 5-fluorouracil and leucovorin was administered during weeks 1 and 5. Treatment response was evaluated 8 weeks after completion of nCRT using pelvic MRI, rigid proctoscopy, and digital rectal examination. Patients achieving clinical complete response (cCR) with distally located tumors were managed with W&W approach, while others proceeded

to surgery 8—14 weeks post-nCRT. DFI was calculated from the date of surgery or, for W&W patients without relapse, from the date of control MRI to the occurrence of progression or last follow-up.

Results: Majority of patients had distally located tumors (80.5%) and stage III disease (96.4%). Extramural vascular invasion (EMVI) on baseline MRI was present in one-third of patients. Sixty-six patients (80.5%) underwent surgery, while 16 (19.5%) were managed with a W&W approach. A favorable response, defined as Mandard tumor regression grade (TRG) 1—2, was observed in 23 patients (28.0%). Median DFI was 33.5 months (range, 1—54), with a 3-year DFI rate of 74.8%. Positive resection margins, unfavorable TRG, presence of a mucinous component, lymphatic, vascular, and perineural invasion, positive nodal status, and the presence of tumor deposits were significantly associated with shorter DFI.

Conclusions: RT dose intensification without chemotherapy intensification doesn't overcome adverse impact of established negative prognostic factors, highlighting the need for personalized treatment strategies particularly in high-risk patients who may benefit from treatment intensification.

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334eP The impact of neoadjuvant therapy for distal rectal cancer on oncological outcomes

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Background: The widespread implementation of total neoadjuvant therapy (TNT) for distal rectal cancer offers hope for improved oncological outcomes, an increase in the number of sphincter-preserving surgeries, and enhanced patient quality of life. Currently, oncological results are being worked out depending on the variant of TNT used.

Methods: A total of 475 patients with stage II-III distal rectal cancer treated from 2021 to 2025 were divided into three groups: Group A (n=112): Induction chemotherapy (6 cycles of FOLFOX) followed by chemoradiotherapy (CRT) and surgery; Group B (n=115): CRT followed by consolidation chemotherapy (6 cycles of FOLFOX) and surgery; Group C (n=248): Standard CRT followed by surgery and adjuvant chemotherapy (4-6 cycles of FOLFOX).The groups showed no statistically significant differences in baseline characteristics. From the initially recruited group A, three patients were excluded due to liver metastases diagnosed before CRT.

Results: The 1:1:2 ratio among groups was not random but reflected the overall patients distribution, influenced by the reduced duration of neoadjuvant therapy due to COVID-19 and wartime condition in Ukraine. Tumor regression rates based on mrTRG were as follows: mrTRG1-3 A:B (72.48% vs. 82.61%), A:C (72.48% vs. 67.34), B:C (82.61% vs. 67.34%); mrTRG4-5 A:B (27.52% vs. 17.39%), A:C (27.52% vs. 32.66%), B:C (17.39% vs. 32.66%), with statistical significance ($p < 0.05$) only between Groups B and C. The percentage of sphincter-preserving surgeries was 79.82% in Group A, 88.69% in Group B, and 74.59% in Group C ($p > 0.05$). Tumor regression based on pTRG: pTRG1-3 A:B (67.89% vs. 77.39%), A:C (67.89% vs. 61.69%), B:C (77.39% vs. 61.69%); pTRG4-5 A:B (32.11% vs. 22.61%), A:C (32.11% vs. 38.31%), B:C (22.61% vs. 38.31%), with statistical significance ($p < 0.05$) only between Groups B and C. Three-year recurrence-free survival rates were: A — 72.48%, B — 76.52%, C — 69.76%, while overall survival rates were: A — 81.65%, B — 86.08%, C — 77.02%, with no statistically significant differences.

Conclusions: The consolidation chemotherapy regimen demonstrated better outcomes, but without statistically significant differences in survival rates. The induction chemotherapy regimen before CRT requires additional restaging.

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335eP Tolerability and safety of adjuvant chemoradiotherapy with S-1 after limited surgery for T1 or T2 lower rectal cancer

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Background: The short-term outcomes of chemoradiotherapy (CRT) with S-1 (a combination of tegafur, gimeracil, and oteracil) following limited surgery for patients with T1 or T2 lower rectal cancer have shown encouraging results. This study was designed to delve deeper into the long-term outcomes of CRT with S-1 after limited surgery, with the goal of evaluating both the long-term efficacy and potential risks associated with this treatment approach in patients diagnosed with T1 or T2 lower rectal cancer.

Methods: This was conducted as a multicenter, single-arm, prospective phase II trial. The patient population consisted of individuals clinically diagnosed with either T1 or T2 lower rectal or anal canal cancer, with a maximum tumor diameter of 30 mm and classified as N0 or M0. Patients underwent local excision or endoscopic resection. After surgery, CRT with S-1 was administered to patients meeting several criteria, including the confirmation of well-differentiated or moderately differentiated adenocarcinoma, negative surgical margins, submucosal invasion depth of ≥1000 μm, and high tumor-budding grade (2/3). The primary endpoint of this study was relapse-free survival, while secondary endpoints included local recurrence-free survival, overall survival, anal sphincter preservation rate, and safety.

Results: A total of 52 patients were included, with pathological diagnoses revealing T1 in 36 patients and T2 in 16 patients. The 3-year and 5-year relapse-free survival rates were 90.17% and 85.87%, respectively. The 3-year and 5-year local recurrence-free survival rates were 90.17% and 88.07%, respectively, while the 3-year and 5-year overall survival rates were 94.03% and 91.94%, respectively.

Conclusions: CRT with S-1 after limited surgery for T1 lower rectal cancer demonstrated favorable outcomes in terms of recurrence, survival, and local control rates while effectively maintaining anal function in patients. However, further treatment approaches may be necessary to improve outcomes for patients diagnosed with stage T2 lower rectal cancer.

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337eP Real-world outcomes of elderly patients with rectal cancer in Guatemala: Evidence from a resource-limited setting

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Background: Rectal cancer is a major cause of cancer morbidity and mortality worldwide. Elderly patients are frequently underrepresented in clinical trials and may receive less aggressive treatment due to comorbidities or concerns regarding treatment tolerance. In low- and middle-income countries, limited access to early diagnosis and multidisciplinary care may further affect outcomes. Data describing rectal cancer outcomes among elderly patients in Guatemala remain scarce. We evaluated clinical characteristics, treatment patterns, and survival outcomes of elderly patients with rectal cancer treated at the Guatemalan Social Security Institute.

Methods: We performed a retrospective cohort study of patients diagnosed with rectal cancer between 2013 and 2018 at the Guatemalan Social Security Institute. Patients were stratified into elderly (≥70 years) and non-elderly (<70 years) groups. Clinical stage at diagnosis, treatment modalities (surgery, chemotherapy, and radiotherapy), and overall survival (OS) were analyzed. Survival was estimated using Kaplan—Meier methods and compared using the log-rank test. Cox proportional hazards models were used to evaluate factors associated with survival.

Results: Eighty-eight patients were included, with a median age of 70 years (±20 years); 71% were male. At diagnosis, 14.3% presented with localized disease, 58.9%