Baseline expression of RAD23B protein in circulating tumour cells correlates with complete pathological response of neoadjuvant chemoradiotherapy for locally advanced rectal cancer

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Background: Neoadjuvant chemoradiotherapy (NCRT) has been consolidated as the main strategy for the treatment of locally advanced rectal cancer (LARC). However, heterogeneous responses are observed, with only about 15-20% of patients presenting a complete pathological response (pCR). This makes it difficult to evaluate. The objective of this prospective study was to analyze whether the protein expression of RAD23 homolog B (RAD23B) in the circulating tumor cells (CTCs) at baseline (before treatment) could correlate with the response to NCRT.

Methods: Between 2016 and 2020, 63 patients (pts) with LARC who underwent NCRT followed by radical surgery were included in the study. Blood samples were collected before the beginning of NCRT (C1) and the evaluation of RAD23B protein expression in CTCs was correlated with the anatomicopathological examination of response of patients undergoing surgery (n=56). CTCs were isolated and quantified by ISET®. RAD23B protein was analyzed by immunocytochemistry and visualized by bright field microscopy.

Results: The mean age was 56 years old (34-92). Among the pts analyzed, 34 (54%) carried the tumor in the right and 31 (46%) in the left rectum. 57 (80%) had clinical tumor stage (C7) T3/T4, 58 (92%) cT3 and 50 (82%) cN positive. The expression of RAD23B was present in 28% of the pts, with a median (IQR) of 188 (26-345) for all pts. In pCR group, it was also observed in 22% of the pts, with a median (IQR) of 134 (55-203). In non-pCR group, it was present in 54% of the pts, with a median (IQR) of 143 (61-345).

Conclusions: This prospective study demonstrated the correlation between the absence of expression of RAD23B in CTCs (C1) and pCR, being an important result for future clinical studies. This analysis may identify NCRT responders candidates, helping to choose the best therapeutic approach for each individual.

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Translation of the IDEA trial into clinical practice: Evaluation of implementation of a new guideline

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Background: The pivotal IDEA trial showed marginal differences in survival outcomes for 3 vs 6 months of adjuvant chemotherapy (ACT) in stage II and III colon cancer (CC). Severe treatment toxicity was substantially lower in the short treatment regimen. Therefore, in 2017 the Dutch colorectal cancer (CRC) guideline was revised and currently recommends 3 months of oxaliplatin (OK)-based ACT. In addition, the definition of high-risk stage II CC was restricted to include only pathological T4 (pT4) tumors (instead of presence of poor differentiation, lymph node harvest <10, lymphovascular invasion and perforation/obstruction at presentation). We evaluated adherence to the revised guideline in The Netherlands.

Methods: From the Netherlands Cancer Registry (NCR) all 16,721 patients ≥18 years with resected high-risk (risk factors according to previous guideline) stage II and III CC treated during 2015-2019 were selected. The impact of implementation of guidelines was analyzed by comparing differences in patient characteristics (Chi-square tests) and in duration of ACT between incidence years (one-way analysis of variance). Treatment patterns and ACT regimens were analyzed according to stage and age.

Results: Of all patients receiving ACT (n=18,170), the proportion treated with CAPOX increased from 75% in 2015/2016 (before guideline revision) to 83% in 2018/2019 (after guideline revision). Intravenous 5-fluorouracil containing ACT was administered in 5% of patients in 2015/2016 and decreased to 2% in 2018/2019. Mean duration of ox-based ACT decreased from 18.6 (± 8.0) weeks in 2015 to 9.5 (± 3.8) weeks in 2019. The proportion of patients receiving ACT was stable over time, 61-69% in stage II and 26-29% in pT4 stage II. ACT in patients with previous high-risk pT3N0 disease decreased from 15% to 3% before and after guideline revision. At the same time the use of ox-based ACT increased from 27% to 49% in patients ≥75 years old.

Conclusions: The revised Dutch CRC guideline, recommending 3 months of ACT and restriction of ACT in stage II to pT4N0 CC, was rapidly implemented in clinical practice. The shortened duration of ACT led to an increase in elderly patients that received ox-based ACT.

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Chemosradiation versus less intensive treatments in stage I squamous cell carcinoma of the anal canal (SCCA)

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Background: Patients (pts) with stage I SCCA are underrepresented in randomized trials of chemoradiation (CRT). While most pts are cured with CRT, this may lead to significant acute and long-term adverse events. Thus less intensive treatments (LT) for these pts could be as effective and less toxic than CRT. We compared the outcomes of real-world stage I SCCA pts treated with CRT versus LT.

Methods: Retrospective study using the population database of FOSP (Fundação Onco-Centro de São Paulo), which collects epidemiological and outcomes data on cancers from 77 hospitals across the state of Sao Paulo, Brazil. Pts with stage I SCCA were eligible. The primary endpoint was to compare disease-free survival (DFS) times between pts treated with CRT (radiation plus chemotherapy with or without adjunctive surgery) and LT (only surgery, radiation or chemotherapy, or surgery and radiation). DFS were compared with the log-rank test and adjusted by a Cox regression model. Logistic regression was used to evaluate factors associated with LT.

Results: From 2000 to 2020, 171 out of 2,401 SCCA pts had stage I tumors and were included. The median time from diagnosis to treatment was 67 days, 131 (76%) was female, median age was 59 years (35-90); 100 pts (58%) received CRT and 71 (42%) LT, with 98 (57%) being treated in the public system. In a median follow up of 43.3 months, 21 (12.2%) pts recurred (12 in CRT and 9 in LT). Median DFS was 39.2 and 24 months for CRT and LT (p=0.057), respectively. Either treatment type (CRT vs LT), sex, age or time from diagnosis to treatment initiation 60 days were associated with DFS. After controlling for sex, health care setting (insurance/private vs public) and treatment location (within or outside of residential city), age 70 years was associated with receipt of LT (OR: 2.34; 95% CI: 1.15 – 4.87; p = 0.019). There was also no difference in DFS (p=0.02) in the subgroup treated with CRT (79) or radiation only (17).

Conclusions: In this large study of real-world stage I SCCA pts, LT was more likely to be offered to older pts and was not associated with inferior DFS when compared to CRT. An organ-preserving LT, such as radiotherapy with or without a fluoropyrimidine, can be considered to older pts with stage I SCCA who are ineligible for CRT.

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The clinical value of C-reactive protein and its association with tumour sidedness in patients undergoing curative surgery for colorectal cancer: A ScotScan collaborative study

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Background: The presence of preoperative systemic inflammatory response (SIR) is an established negative prognostic factor for patients diagnosed with colorectal cancer (CRC). C-reactive protein (CRP) is known to be implicated in detrimental immune responses. The biological differences between right-sided and left-sided CRC are...